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Impacto dos Internamentos de Adultos por Pneumonia Adquirida na Comunidade, em Portugal Continental

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"*Everything should be made as simple as possible,*
but not simpler."

Albert Einstein (1879-1955)

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Resumo

Introdução

Estima-se uma incidência anual de 5 a 11 casos de Pneumonia Adquirida na Comunidade (PAC) por 1.000 habitantes adultos, o que permite extrapolar para Portugal valores próximos dos 50.000 a 100.000 casos anuais.

A incidência da PAC aumenta com a idade, sendo, igualmente, mais frequente no Inverno, nos homens e na presença de múltiplos fatores de risco, tais como, o álcool, o tabaco, as doenças respiratórias crónicas, a insuficiência renal e a malnutrição. Nas comorbilidades, merece destaque o aumento na Doença Pulmonar Obstrutiva Crónica (DPOC).

Na União Europeia, todos os anos, ocorrem aproximadamente 1 milhão de internamentos de adultos por PAC. A taxa de hospitalização varia entre 20 a 50% nos diferentes países, refletindo variações climáticas, nas populações avaliadas e, sobretudo, nas organizações dos sistemas de saúde. Estes valores correspondem a incidências anuais dos internamentos de adultos por PAC de 1,1 e 4,0 internamentos por 1.000 habitantes. Na Europa, sobretudo nos países do Norte, tem-se verificado um aumento da incidência dos internamentos, sobretudo na população idosa.

Globalmente, as infeções respiratórias inferiores, que incluem a PAC, foram a 4ª causa de morte em 2015. Estima-se que a pneumonia seja responsável por 3,2 milhões de mortes anuais a nível mundial. Nos países desenvolvidos, a PAC é a primeira causa de morte por doença infeciosa e a quase totalidade das mortes refere-se à letalidade intra-hospitalar. A mortalidade por CAP pode variar entre 1 e 48%, de acordo com países e populações estudadas, com vários fatores associados a um acréscimo significativo de mortalidade, tais como, a idade, a gravidade e as comorbilidades.

A abordagem dos doentes com PAC está associada a importantes custos diretos, indiretos e intangíveis no ambulatório e, sobretudo, a nível hospitalar. Na União Europeia, os custos anuais da PAC foram estimados em 10 biliões de Euros, dos quais €5,7 biliões em internamentos hospitalares, €0,5 biliões em cuidados de ambulatório, €0,2 biliões em fármacos e €3,6 biliões em custos indiretos pela perda de dias de trabalho. Independente da região ou população estudada, verifica-se uma enorme diferença entre os custos dos doentes tratados em ambulatório e em regime hospitalar, A decisão da escolha do local de tratamento, em internamento ou em ambulatório. revela-se, assim, uma decisão crítica no prognóstico e na alocação de recursos.

A dimensão do impacto da PAC e o seu previsível incremento exponencial em resultado do envelhecimento da população, do aumento da prevalência das doenças crónicas não transmissíveis e da crescente ameaça das resistências aos antimicrobianos, contextualizam esta entidade nosológica com um importante problema de saúde individual e, sobretudo, de saúde pública. Justifica-se, assim, uma maior sensibilização e adesão da população e, em particular, dos grupos de maior risco, às medidas de promoção de saúde e de prevenção da doença. No âmbito da PAC, estas medidas incluem a intervenção nos fatores de risco associados e estilos de vida, bem como o reforço da cobertura vacinal contra a gripe e infeções pelo *Streptococcus pneumoniae*.

Na presente tese pretende-se caracterizar o impacto dos internamentos de adultos por PAC em Portugal continental tentando-se responder aos seguintes objetivos principais e secundários:

1. Objetivos principais:
    1.1. Incidência dos internamentos de adultos por PAC em Portugal continental
    1.2. Letalidade intra-hospitalar dos internamentos de adultos por PAC em Portugal continental
    1.3. Custos diretos dos internamentos de adultos por PAC em Portugal continental
2. Objetivos secundários
    2.1. Papel dos médicos na decisão crítica de internamento hospitalar por PAC
    2.2. Importância das medidas de promoção da saúde e de prevenção da doença na redução do impacto dos internamentos de adultos por PAC em Portugal continental

Metodologia

Esta tese consistiu na publicação de 8 artigos em revistas indexadas (4 internacionais e 4 nacionais), com *peer-review* e fatores de impacto entre 13.204 e 0.281, à data da publicação. Estes artigos, a 30/06/2018, já tinham sido citados 50 vezes noutras publicações. Três artigos são estudos retrospetivos, dois são artigos de revisão, dois são artigos de opinião publicados no formato de editorial e um artigo é um documento de consenso com o patrocínio de uma sociedade científica portuguesa.

Os três artigos retrospetivos analisaram, no período de 2000 a 2009, a base de dados da Administração Central do Sistema de Saúde (ACSS), do Ministério de Saúde, que contém os dados administrativos e clínicos de todas as admissões nos hospitais do

Serviço Nacional de Saúde (SNS), que abrange quase toda a população residente em Portugal continental no período analisado. Foram selecionados retrospetivamente todos os internamentos de adultos com o diagnóstico principal de Pneumonia (ICD9: 480 a 486 e 487.0). Excluíram-se os doentes menores de 18 anos e doentes com pneumonia como diagnóstico não principal e os internamentos de doentes infetados com o vírus da imunodeficiência humana (VIH) (ICD9: 042 a 044 e GDH: 488, 489 e 490), imunocomprometidos por antineoplásicos ou imunossupressores (causa externa de doença: código E933.1) e transplantados (V42). Na análise da informação clínica foi assegurado o anonimato dos doentes. Os métodos estatísticos utilizados em cada um dos artigos estão discriminados no respetivo estudo. Apesar das limitações, a metodologia utilizada tem sido considerada válida e aplicada em múltiplos estudos realizados em diferentes países.

Resultados

No período de 2000 a 2009, foram avaliados 294.027 internamentos de adultos com o diagnóstico principal de PAC. Os internamentos ocorreram predominantemente em homens (56%) e idosos, com uma média de idade dos doentes internados de 73,1 anos. Constatou-se um aumento do número de internamentos em todos os grupos etários, mais marcado nas idades ≥65 anos. Estes internamentos representam 3,7% do total de internamentos de adultos no SNS, aumentando para 7,0% na população com idade ≥65 anos. Estes valores correspondem a uma incidência média anual de 3,61 internamentos por 1.000 habitantes e de 13,40 por 1.000 na população com idade ≥65 anos. De 2000 a 2004 para 2005 a 2009, a incidência aumentou 28,3%, de 3,16 para 4,05 por 1.000 habitantes.

Ocorreram 59.925 óbitos, o que equivale a uma taxa de letalidade intra-hospitalar de 20,4%. A letalidade aumentou significativamente com a idade, com valores médios de 5,0% nos doentes com idade <50 anos e de 24,1% nos doentes com idade ≥65 anos. A letalidade aumentou ao longo dos dez anos estudados, mesmo após ajustamento para a idade e sexo. A média das idades dos doentes falecidos foi de 79,8 anos e os doentes com idade ≥50 anos apresentaram um risco relativo de morte intra-hospitalar de 4,4 comparando com os doentes com idade <50 anos. Os homens morreram mais e mais jovens do que as mulheres, com um risco relativo de falecerem 17% mais elevado em relação às mulheres.

Nos cálculos dos custos diretos foram incluídos todos os doentes internados, englobando os internamentos em UCI. A média anual e diária dos custos diretos foi de

80 milhões de euros e 218.050 euros, respetivamente, com uma tendência crescente ao longo dos anos. Cada internamento teve um custo direto médio de 2.706 euros.

Atendendo ao significativo impacto no prognóstico e na alocação de recursos, propõe-se que a decisão de internamento de adultos com PAC seja feita por médicos com maior experiência e diferenciação (SMART-DOCTORS).

Para a atuação em fatores de risco associados a estilos de vida, sugerimos a utilização de um acrónimo simples e de fácil memorização, o ATCHIN, que aglutina um conjunto de intervenções (Álcool, Tabaco, controlo das Comorbilidades, Higiene oral, terapêuticas Imunossupressoras e estado Nutricional) com implicações significativas no risco das pneumonias.

Na prevenção das pneumonias merece destaque o reforço da implementação das normas e orientações da Direção-Geral da Saúde (DGS) de vacinação contra a gripe e as infeções pelo *Streptococcus pneumoniae*. O maior envolvimento das sociedades científicas, nomeadamente da Sociedade Portuguesa de Pneumologia, pode contribuir para um aumento da consciencialização do problema das infeções respiratórias e da importância da sua prevenção na gestão da doença quer juntos dos profissionais de saúde, quer da população e, em particular, nos doentes com DPOC.

Conclusões

Os dados apurados neste estudo, que analisa o período de 2000 a 2009, permitem fundamentar que em média, em Portugal continental, verificam-se 81 internamentos de adultos por PAC por dia, o que corresponde a um internamento a cada 18 minutos. Nestes 81 internamentos diários, ocorre o óbito em 16 doentes, um óbito a aproximadamente cada 90 minutos. E os custos diretos dos internamentos representam um milhão de euros a cada 4 dias e 14 horas.

Tendo em consideração o impacto no prognóstico e nos custos, a decisão de internar adultos com PAC deve ser feita por médicos com maior experiência e diferenciação.

A dimensão dos internamentos de adultos por PAC no nosso país, justifica totalmente a intervenção nos principais fatores de risco associados a estilos de vida e uma maior sensibilização da população e dos profissionais de saúde para o aumento das taxas de cobertura vacinal contra a gripe e as infeções por *Streptococcus pneumoniae*.

Palavras-Chave: Pneumonia; Pneumonia adquirida na comunidade; Internamentos; Incidência; Mortalidade; Letalidade; Custos; Prevenção.

Abstract

Introduction

There is an estimated annual incidence of Community Acquired Pneumonia (CAP) of 5 to 11 cases per 1.000 adult inhabitants, which can be extrapolated to 50.000 to 100.00 annual cases in Portugal.

The incidence of CAP increases with age and it is more common in Winter, in males and in the presence of several risk factors, such as alcohol, smoking, chronic respiratory disease, renal failure and malnutrition. Regarding comorbidities Chronic Obstructive Pulmonary Disease (COPD) should be particularly highlighted.

There are approximately 1 million adult hospital admissions in the European Union for CAP annually. Hospitalization varies between 20 to 50% in different countries, which reflects weather variations, differences in populations and, above all, differences in the organization of healthcare provision. These data correspond to an annual incidence of admissions for CAP in adults of 1.1 to 4.0 admissions per 1,000 inhabitants. In Europe, particularly in Northern European countries, there is a trend towards increasing admissions for CAP, particularly among the elderly. Globally, respiratory infections, which include CAP, were the 4th leading cause of death in 2015.

It is estimated that, every year, pneumonia accounts for 3.2 million deaths globally. In developed countries, CAP is the leading cause of death by infectious disease and nearly all deaths are related to intra hospital lethality. CAP mortality varies between 1 to 48% according to countries and studied populations, with several factors associated with increasing mortality such as age, severity and comorbidities. The management of patients with CAP is associated with significant direct, indirect and intangible costs in the primary cares setting but above all in the hospital setting. In the European Union the direct annual costs of CAP have been estimated in 10 million euros, of which €5.7 billion are for hospital admissions, €0.5 billion for primary care, €0.2 billion in drugs and €3.6 billion in indirect costs due to working days lost. Irrespective of region or population studied there is an enormous difference between the cost of patients treated in the community and those who require hospital admission. The decision regarding the place of treatment, hospital admission or community setting, is therefore of extreme importance in the prognosis and resource allocation.

The increase age of our population, together with the increase in chronic non-transmissible diseases and the growing threat of antimicrobial resistance leads to an

increase in the dimension of CAP impact making this an individual and, above all, public health problem.

It is therefore necessary a greater advocacy for health promotion and disease prevention, particularly in higher risk groups. Regarding CAP these include intervening in lifestyle associated risk factors and increasing immunization cover against influenza and *Streptococcus pneumoniae*.

The present thesis aims to characterize the impact of CAP admissions in adults in mainland Portugal. It will strive to answer the following primary and secondary objectives:

1. Primary Objectives:
    1.1. Hospital admissions for CAP in adults in mainland Portugal
    1.2. Intra-Hospital lethality in hospital admissions in adults with CAP in mainland Portugal
    1.3. Direct costs of hospital admissions for CAP in adults in mainland Portugal.
2. Secondary Objectives
    2.1. The role of doctors in the critical decision regarding hospital admission for CAP
    2.2. The importance of health promotion and disease prevention in reducing the impact of CAP admissions in adults in mainland Portugal

Methodology

This thesis consisted in 8 publications in indexed journals (4 international and 4 national) with *peer-review* and impact factors between 13.204 and 0.281, at the time of publication. These publications had, by 30th June 2018, been quoted 50 times in other publications.

These publications are three retrospective studies, two are review articles, two are opinion articles published in the editorial format and one is a consensus article sponsored by a Portuguese scientific society.

The three retrospective articles analysed the Central Administration of the Health Service (ACSS) and the Ministry of Health database between 2000 a 2009. This database contains administrative and health data of all hospital admissions in the National Health Service which includes nearly all resident population in mainland Portugal during the studied period. All hospital admissions of adults admitted with the main diagnosis of pneumonia (ICD9: 480 a 486 e 487.0) were retrospectively selected. Patients younger than 18 years old were excluded, as well as those whose main diagnosis was not

pneumonia, those infected with human immunodeficiency virus (ICD9: 042 a 044 e GDH: 488, 489 e 490), the immunosuppressed by anti-neoplastic drugs, immunosuppressants (external disease cause: code E933.1) and transplanted patients (V42).

Patients anonymity was guaranteed throughout analysis of clinical data. The statistical method used in each study is specified in the referred study. Despite its limitations this methodology has been used and validated in different studies form different countries.

Results

Between the years 2000 and 2009 there were 294,027 hospital admissions of adults whose main diagnosis was CAP. Admissions were more common in males (56%) and in the elderly, mean age of admitted patients 73.1 years. There was an increase in admission in all age groups, though more significant in age ≥65 years. These admissions correspond to 3.7% of all hospital admission in the National Health Service, which increases to 7.0% in the population older than 65 years.

These hospital admissions correspond to a mean annual incidence of 3.61 admissions per 1,000 inhabitants, and 13.40 per 1,000 inhabitants in those older than 65 years. Between 2000 to 2004 and 2005 to 2009 there was a 28.3% increase in admissions, from 3.16 to 4.05 per 1,000 inhabitants.

There were 59,925 deaths, which corresponds to intra hospital lethality of 20.4%. Lethality increased significantly with age, mean values of 5.0% in patients younger than 50 years and 24.1% in patients older than 65 years.

After correcting for age and gender, lethality increased throughout the ten-year studied time frame. The mean age of deceased patients was 79.8 years and patients older than 50 years had a relative risk of intra hospital death of 4.4 when compared with patients younger than 50 years. Males died more and at a younger age than females. Males had a relative risk of dying 17% higher than females.

Calculation of direct costs included all admitted patients, including patients admitted to ICU. The annual and daily average of direct cost was 80 million euros and 218,050 euros respectively, and with a trend towards increasing cost through the years. Each hospital admission had a mean direct cost of 2,706 euros.

Considering the significant impact of prognosis and resource allocation, we propose that the decision to admit adults with CAP should be made by doctors with greater experience and expertise (SMART-DOCTORS).

In addressing lifestyle associated risk factors we propose a simple and easy acronym ATCHIN, which includes a bundle of interventions (Alcohol, Tobacco/smoking cessation, control of comorbidities, oral Hygiene, Immunosuppressive treatments and Nutritional status) which carries significant implication in the risk of pneumonia.

Considering pneumonia prevention, we highlight the implementation of the General Directorate of Health (Direção-Geral da Saúde) guidelines regarding immunization against influenza and *Streptococcus pneumoniae*. A greater participation of scientific societies, such as the Portuguese Pulmonology Society, can contribute to a better understanding of the risk associated with respiratory infections. It is also important to acknowledge the importance of preventing respiratory infections in managing these, be it among health professionals, the population and, in particular, COPD patients.

Conclusions

Data acquired in this study, which analysis the period between 2000 and 2009 allow us to state that, on average, in mainland Portugal, there are 81 hospital admission for CAP per day. This corresponds to one admission every 18 minutes. In these 81 daily admissions, there is one death in 16 patients, approximately one death every 90 minutes. The direct costs of hospital admissions represent one million euros every 4 days and 14 hours. The decision to admit to hospital adults with CAP has an impact both on prognosis and cost, hence this decision should be made by doctors with experience and expertise.

The dimension of adult admissions with CAP in our country completely validates the need in intervening in lifestyle associated risk factors, as well as and a greater education of our population and health care professionals for an increase in immunization cover against influenza and *Streptococcus pneumoniae*.

Keywords: Pneumonia; Community Acquired Pneumonia; Hospital admissions; Incidence, Mortality; Lethality; Costs; Prevention.

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Abreviaturas e Acrónimos

ACSS: Administração Central do Sistema de Saúde

BTS: *British Thoracic Society*

CURB-65: *Confusion*, *Urea*, *Respiratory rate*, *Blood pressure*, age ≥65 anos

DGS: Direção-Geral da Saúde

DPOC: Doença Pulmonar Obstrutiva Crónica

EUA: Estados Unidos da América

GDH: Grupos de Diagnóstico Homogéneo

ICD-9-CM ou **ICD9**: *International Classification of Diseases, Ninth Revision, Clinical Modification*

N/A: Não Aplicável

PAC: Pneumonia Adquirida na Comunidade

***PSI**: Pneumonia Severity Index*

SCAP: *Severe* CAP

SMART-COP: *Systolic blood pressure*, *Multilobar infiltrates*, *Albumin*, *Respiratory rate*, *Tachycardia*, *Confusion*, *Oxygen* and pH

SNS: Serviço Nacional de Saúde

UCI: Unidade de Cuidados Intensivos

VIH: Vírus da imunodeficiência Humana

VPC13: Vacina Pneumocócica Conjugada 13 valente

VPP23: Vacina Pneumocócica Polissacarídica 23 valente

Esta listagem não referencia as figuras, tabelas, abreviaturas e acrónimos dos artigos publicados.

1. Introdução

A PAC é uma doença comum e frequente, que pode afetar adultos de todos os grupos etários, incluindo jovens imunocompetentes e previamente saudáveis. O diagnóstico de pneumonia é transversal a todas as especialidades médicas.

A história da PAC acompanha a história da Humanidade. Em 1881, Louis Pasteur (1822-1895) (1) e George Miller Sternberg (1838-1915) (2) a trabalharem separadamente descreveram um microrganismo que Albert Fraenkel (1848-1916), posteriormente, designou como Pneumococcus (3) por causar doença pulmonar. Antes do advento da antibioterapia, o Pneumococcus ou *Streptococcus pneumoniae*, como atualmente é também designado, era responsável por mais de 75% das pneumonias (4).

No início do século XX, William Osler (1849-1919), um dos principais impulsionadores da medicina moderna, cunhou a entidade clínica de pneumonia como o "Capitão dos homens da morte" (5), vindo a falecer de pneumonia, muito provavelmente pneumocócica, a 29 de dezembro de 1919 durante a pandemia de gripe espanhola.

A necessidade de combater a ameaça da pneumonia contribuiu para muitos avanços da medicina e da saúde pública. A procura do tratamento para a pneumonia foi responsável pelos primeiros tratamentos com soroterapia (6), o primeiro estudo "controlado" de eficácia da antibioterapia (7) e foi determinante no desenvolvimento de novos fármacos antimicrobianos e de vacinas. Todos estes desenvolvimentos tiveram um profundo impacto na melhoria do prognóstico global das doenças infeciosas e no aumento da esperança média de vida da população.

Contudo nas últimas décadas, a par do envelhecimento da população, do aumento da prevalência das doenças crónicas não transmissíveis, do crescimento das resistências aos antimicrobianos nos microrganismos tradicionais, como é o caso das resistências do Pneumococcus à penicilina e aos macrólidos, e da identificação de novos patogenos responsáveis por PAC (exemplo, SARS, MERS-CoV), não se verificaram alterações significativas na abordagem terapêutica da PAC. Em face desta realidade, a PAC persiste como um importante problema de saúde pública, com elevada morbilidade, mortalidade e consumo de recursos de saúde (8), representando a segunda causa de anos de vida perdidos após a doença isquémica cardíaca (9).

Revela-se, assim, da maior pertinência a avaliação do impacto da PAC em Portugal e, em particular, na sua vertente de internamentos hospitalares, que representam a quase totalidade da mortalidade e do consumo de recursos. Por exemplo, e de acordo com a

British Thoracic Society (BTS), a percentagem de adultos com PAC que necessitam de internamento no Reino Unido varia entre 22 e 44% (10), com estudos na Finlândia e Espanha a apresentar valores entre os 42% (11) e os 50% (10), respetivamente. Como seria de esperar, a mortalidade é variável de acordo com a gravidade que condiciona a escolha do local de tratamento, com valores médios em diferentes países europeus de cerca de 1% em ambulatório, 5 a 15% no internamento hospitalar e mais de 40% nos doentes admitidos em Unidades de Cuidados Intensivos (UCI) (12).

Relativamente aos custos do tratamento da PAC, vários estudos europeus e norte-americanos apontam para custos diretos dos internamentos hospitalares superiores a 85% do total dos custos (13,14), o que releva, igualmente, a importância de na análise dos custos da PAC em Portugal se tenha que incluir, necessariamente, os internamentos hospitalares.

Com esta tese de doutoramento pretende-se, assim, avaliar o impacto dos internamentos de adultos por PAC em Portugal continental, nomeadamente através da determinação da incidência dos internamentos, da letalidade intra-hospitalar e dos respetivos custos diretos. Embora os internamentos hospitalares representem uma percentagem variável e não determinada no nosso país do número total de casos de PAC, que se estima entre os 25 e os 50%, os episódios de internamento são responsáveis pela quase totalidade da mortalidade e dos custos associados à PAC. O facto de se analisar um período temporal alargado, neste caso de 10 anos, contribui igualmente para diminuir o impacto de variações climáticas, da ocorrência de fenómenos anormais ou extraordinários decorrentes de surtos e alterações sazonais ou anuais na circulação de microrganismos, tais como, por exemplo, *Mycoplasma pneumoniae*, bactérias do género *Legionella* e vírus respiratórios, nomeadamente o vírus influenza.

Finalmente e ainda no contexto da abordagem terapêutica da PAC, verifica-se um outro problema da maior relevância para a saúde pública. As pneumonias são uma importante causa de consumo de antibióticos e o consumo destes fármacos é o principal fator de desenvolvimento e perpetuação das resistências. As resistências aos antimicrobianos constituem um dos maiores problemas de saúde pública com que nos deparamos no presente e no futuro. Se esta situação não for alterada existem previsões que, em 2050, as resistências aos antimicrobianos sejam responsáveis por mais de 10 milhões de óbitos a nível mundial, um óbito a cada 3 segundos, e mais mortalidade do que a resultante de doenças neoplásicas e diabetes (15).

Este estudo é inovador e vem colmatar uma importante lacuna do conhecimento no nosso país, podendo contribuir para uma melhor gestão desta entidade clínica, da alocação de recursos e fundamentar um acréscimo da necessidade da implementação de medidas preventivas.

No nosso país e desde há muitos anos existe informação centralizada numa base de dados nacional com a codificação das notas de alta hospitalar, baseada na Classificação Internacional das Doenças, 9ª Revisão, Clinicamente Modificada (ICD-9-CM, *International Classification of Diseases, Ninth Revision, Clinical Modification*). A codificação é assegurada por médicos com formação específica e sujeita a auditorias internas e externas. Esta base de dados revela-se uma ferramenta da maior utilidade na avaliação do impacto dos internamentos hospitalares de adultos com o diagnóstico principal de pneumonia. De igual modo, a inexistência de registos de codificação centralizados, fidedignos e uniformes nos cuidados de saúde primários, inviabilizam a extensão desta análise aos doentes seguidos em ambulatório. Finalmente, a impossibilidade de aceder aos registos dos internamentos hospitalares das regiões autónomas da Madeira e dos Açores, limitam a análise a Portugal continental, sem pôr, de modo algum, em causa a representatividade da amostra populacional residente no nosso país.

O estudo baseia-se na análise retrospetiva da base de dados relativa a Portugal continental e que é gerida pela ACSS, do Ministério de Saúde. Esta base de dados contém dados administrativos e clínicos de todas as admissões nos hospitais do SNS, que abrange quase toda a população residente em Portugal continental. A informação clínica, incluindo os diagnósticos e os procedimentos, é codificada a partir das notas de alta dos internamentos hospitalares por médicos com formação específica, de acordo com a ICD-9-CM, durante o período em análise.

Neste estudo, foram selecionados retrospetivamente todos os internamentos com o diagnóstico principal de Pneumonia (ICD9: 480 a 486 e 487.0), no período compreendido entre 2000 a 2009. Os códigos utilizados excluem as formas de pneumonia tuberculosa ou pneumonia obstrutiva associada, por exemplo, a neoplasia do pulmão. Excluíram-se ainda os doentes menores de 18 anos e doentes com pneumonia como diagnóstico não principal. Como a ICD-9-CM não especifica se a pneumonia é adquirida na comunidade, excluíram-se também os doentes com infeção VIH (ICD9: 042 a 044 e GDH: 488, 489 e 490), imunocomprometidos por antineoplásicos ou imunossupressores (causa externa de doença: código E933.1) e transplantados (V42). Na análise da informação clínica, os dados foram anonizados, sendo, assim, garantido o anonimato dos doentes.

É, igualmente, nosso objetivo fundamentar que os dados encontrados são muitos significativos em termos de morbilidade, mortalidade e consumo de recursos de saúde com importante impacto a nível da saúde individual e da saúde pública. A implementação de medidas de promoção da saúde e de prevenção da doença, como a literacia e a capacitação em saúde e o envelhecimento saudável revelam-se, deste modo, cruciais no âmbito das infeções respiratórias, em particular, das pneumonias. Justificam-se amplamente medidas de intervenção em fatores de risco associados a estilos de vida, bem como o reforço das coberturas vacinais contra a gripe e as infeções a *Streptococcus pneumoniae*, para os quais já existem documentos orientadores e normativos da DGS.

Esta tese de doutoramento está estruturada no conhecimento e caracterização de três variáveis principais: a incidência, a letalidade intra-hospitalar e os custos diretos dos internamentos de adultos por PAC em Portugal continental. O conhecimento e a caracterização destas variáveis numa população cada vez mais idosa e mais doente, a traduzir um aumento da esperança média de vida e da prevalência das doenças crónicas não transmissíveis, justificam a inclusão de medidas de promoção da saúde e de prevenção da doença, nomeadamente ao nível da intervenção nos fatores de risco associados a estilos de vida e à vacinação antigripal e antipneumocócica.

Tendo em consideração a estrutura da tese em artigos publicados, esta tese é bilingue (português e inglês) e o seu formato promove alguma repetição de conteúdos.

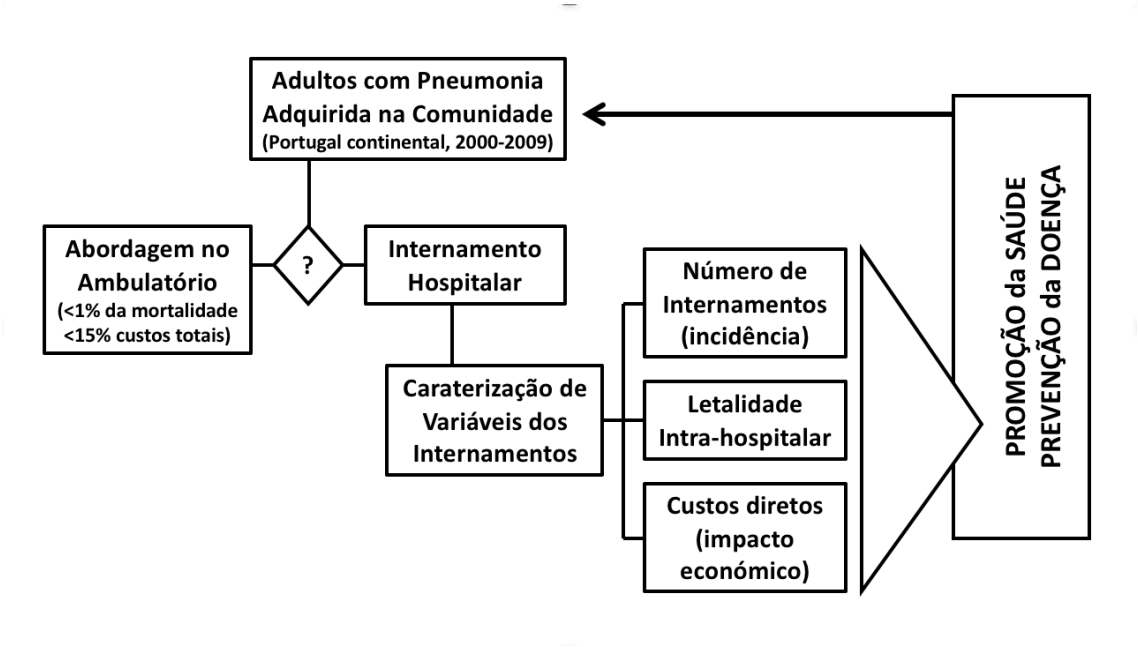

Figura 1 – Esquema conceptual da tese de doutoramento.

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2. Revisão crítica da literatura

2.1. Incidência da Pneumonia Adquirida na Comunidade

A incidência de uma doença mede o número de novos casos de doença que ocorrem numa população num determinado período de tempo. Em relação à pneumonia, existem várias limitações na determinação da incidência em resultado das populações estudadas (por exemplo, faixas etárias, comorbilidades, grau de autonomia), períodos de tempo analisados e meios de diagnóstico utilizados na confirmação diagnóstica. A maioria dos doentes são tratados em ambulatório, onde nem sempre se procede à confirmação radiológica do diagnóstico (1).

Estudos prospetivos anteriores a 1987 e realizados nos Estados Unidos da América (EUA) e em países do norte da Europa estimaram uma incidência anual de 5 a 11 casos de PAC por 1.000 habitantes adultos (2-4). Com base nestes dados é possível extrapolar para Portugal valores próximos dos 50.000 a 100.000 casos de PAC por ano.

A incidência é maior no Inverno, nos idosos, nos homens e na presença de múltiplos fatores de risco, tais como, o álcool, o tabaco, as doenças respiratórias crónicas, a insuficiência renal e a malnutrição (5). Múltiplos estudos documentam o aumento da incidência da PAC com a idade. Num dos estudos pioneiros na Finlândia, a incidência anual foi de 6 por 1.000 entre os 16 e os 59 anos, de 15,4 por 1.000 entre os 60 e os 74 anos e de 34,2 por 1.000 nos com idade ≥75 anos (3). Um aumento de seis vezes na incidência entre os indivíduos com idade entre os 16-59 anos em comparação com os de idade ≥75 anos (3).

De igual modo, estudos realizados em diferentes países europeus confirmam a maior incidência de PAC no género masculino, quer no ambulatório, quer em internamento hospitalar. Em Espanha um estudo realizado no ambulatório, entre 1993 e 1995, revelou diferenças em todos os grupos etários com valores na incidência anual por 1.000 habitantes de 1,2 nos homens e 1,0 nas mulheres com idades entre os 15-39 anos, 1,8 e 1,4 entre os 40-64 anos e 5,2 e 1,9 nas idades ≥64 anos (6).

O acréscimo de incidência nos doentes com comorbilidades está, igualmente, profusamente documentado em inúmeros estudos. Dentro destes estudos, merece maior destaque o aumento da incidência na DPOC com valores de 22,4 por 1.000 pessoas-ano (7).

2.2. Incidência dos internamentos hospitalares por PAC

A taxa de hospitalizações por PAC varia entre países, refletindo diferentes populações, variações climáticas e na organização dos sistemas de saúde com valores entre os 20 e os 50% do total de casos de PAC (8) e a que correspondem incidências anuais entre o 1,1 e os 4,0 internamentos por 1.000 habitantes (1).

Em termos globais, na União Europeia ocorrem aproximadamente 1 milhão de internamentos de adultos por PAC anualmente (8). Nos EUA, a incidência anual dos internamentos por PAC foi recalculada entre 2010 e 2012 em 24,8 por 10.000 (9), um valor ligeiramente inferior ao calculado em 1991 de 26,7 por 10.000 adultos (10). Esta ligeira diminuição é contrária ao aumento dos internamentos por PAC que se documentaram em vários países europeus, nomeadamente no Reino Unido (11), Alemanha (12) e Dinamarca (13). No Reino Unido, a incidência padronizada por idade aumentou em 34% entre 1997-98 e 2004-05, sobretudo na população mais idosa e o aumento da incidência dos internamentos nos homens foi de 7% em relação às mulheres (11). Na Alemanha, a incidência aumentou 7,6% entre 2005 e 2006, correspondendo a valores de 2,75 e de 2,96 internamentos por 1.000 habitantes/ano, respetivamente (12). Este estudo veio, ainda, corroborar o aumento significativo da incidência com a idade, com valores de 7,65 por 1.000 habitantes/ano nos doentes com idade >60 anos e maior incidência no género masculino, 3,21 versus 2,52 por 1.000 nas mulheres (12). Na Dinamarca, verificou-se um aumento entre 1994 e 2003 de 2,8 para 4,4 internamentos por 1.000 habitantes/ano (13).

A importância da idade foi, igualmente, documentada em países do sul da Europa. Em Espanha, num estudo realizado na Catalunha entre 2002 e 2005, a incidência dos internamentos na população com idade ≥65 anos de foi 10,5 por 1.000 pessoas ano (14).

No nosso país, no primeiro estudo plurianual e de abrangência nacional sobre a incidência de internamentos por PAC, o período analisado foi de 1998 a 2000 (15). Neste estudo, os internamentos por PAC representaram 3,0% do total de internamentos de adultos em Portugal continental, com uma média da incidência anual de 2,66 internamentos por 1.000 habitantes. Este valor aumentou para 9,78 por 1.000 no grupo etário com idade ≥65 anos. De registar uma média de idade dos doentes internados de 69,8 anos, com 71,6% dos doentes com idade ≥65 anos (15). Como se pode constatar, os valores encontrados no estudo português estão dentro dos limites de referência dos estudos realizados no mesmo período de tempo noutros países de semelhante nível de desenvolvimento. Estes dados confirmam o impacto significativo dos internamentos por

PAC no nosso país já nos finais do século passado. E justificam a necessidade de uma melhor caracterização da situação atual que permita corroborar, à semelhança do verificado noutros países europeus, o aumento destes episódios de internamento em resultado do aumento da esperança média de vida.

2.2.1. Decisão de internamento e estratificação da gravidade

Pelo impacto no prognóstico, no consumo de recursos e, consequentemente, nos custos associados, a decisão de internar ou tratar em segurança no ambulatório é da maior pertinência e atualidade. Vários scores ou índices foram desenvolvidos para ajudar os médicos na decisão de internamento com base na identificação dos doentes com muito baixo de risco de mortalidade, sem necessidade de internamento hospitalar e com indicação para tratamento em segurança no ambulatório.

Os dois scores mais conhecidos e utilizados são *Pneumonia Severity Index* (PSI) e o CURB-65. O PSI estratifica os doentes com PAC em 5 classes de risco de acordo com a avaliação de 19 parâmetros demográficos, clínicos e laboratoriais (16). A elevada ponderação da idade e das comorbilidades e a complexidade do PSI conduziu ao desenvolvimento pela BTS de um outro score, o CURB-65, correspondente ao acrónimo para *Confusion*, *Urea*, *Respiratory rate*, *Blood pressure* e idade ≥65 anos (17). A cada alteração corresponde um ponto e doentes com CURB-65 de 0 ou 1 pontos têm um risco de mortalidade de 1,5%, podendo ser tratados no ambulatório em segurança (17).

Nos doentes internados, a necessidade de uma correta e precoce estratificação da gravidade de modo a permitir uma mais célere referenciação para as UCI levou ao desenvolvimento de outros índices ou scores, nomeadamente o SMART-COP (acrónimo para *Systolic blood pressure*, *Multilobar infiltrates*, *Albumin*, *Respiratory rate*, *Tachycardia*, *Confusion*, *Oxygen* and pH) (18) e o SCAP (*Severe* CAP) (19).

Vários estudos avaliaram a utilidade e o valor preditivo dos diferentes scores. O PSI e CURB-65 são os scores mais extensamente e melhor estudados, tendo tido resultados comparáveis na identificação dos doentes de baixo risco, embora num estudo o CURB-65 tenha tido melhores resultados na predição de mortalidade em doentes mais graves (20). Estudos mais recentes, sugerem que a inclusão de marcadores inflamatórios de fase aguda, por exemplo, a proteína C-reactiva ou a procalcitonina, pode melhorar o valor preditivo destes scores (20).

Contudo, nem o PSI nem o CURB-65 têm em consideração fatores sociais, estado funcional, graus de dependência e, na avaliação das comorbilidades, a presença de DPOC ou imunossupressão. De igual modo, nenhum dos scores está validado em

populações de doentes residentes em Portugal. Estas circunstâncias não inviabilizam a utilização dos scores, contudo devem exigir maior prudência e atenção na avaliação do caso clínico específico e único que cada doente apresenta de modo a fundamentar com mais adequação e segurança a decisão de tratar em ambulatório ou em internamento hospitalar.

2.3. Mortalidade e Letalidade intra-hospitalar por PAC

Globalmente, as infeções respiratórias inferiores, que incluem a PAC, foram a 4ª causa de morte a nível mundial em 2015 (21). Estima-se que a pneumonia seja responsável por 3,2 milhões de mortes anuais a nível global, um número que excede todas as outras infeções incluindo a tuberculose, infeção VIH e malária (22). De referir que, embora alguns progressos tenham sido feitos, a diminuição das mortes por pneumonia é significativamente inferior aos resultados obtidos noutras infeções, como na diarreia, infeção VIH e malária (22).

Nos países desenvolvidos, a PAC é a primeira causa de morte por doença infeciosa (23) e foi a 8ª causa de morte global nos EUA, em 2014 (24). A quase totalidade das mortes por PAC nos países desenvolvidos refere-se à letalidade intra-hospitalar atendendo a que a mortalidade dos doentes em ambulatório é <1% (25,26).

Na Europa, a mortalidade por CAP varia muito entre diferentes países. Numa meta-análise publicada em 2012 (27), foram registados valores entre 1% e 48% com vários fatores associados a um acréscimo de mortalidade, tais como, a idade (≥65 anos), necessidade de UCI, uso de corticosteroides, microrganismo atípico, comorbilidades, insuficiência renal aguda e alterações do estado de consciência. Estas variações na mortalidade por PAC traduzem-se em taxas de mortalidade padronizadas pela idade entre 4,5 a 5 por 100.000 na Turquia, 30 a 35 por 100.000 habitantes no Reino Unido e 38,3 por 100.000 na Eslováquia (8). Ainda no Reino Unido a letalidade intra-hospitalar documentada pela BTS varia entre os 8 e os 14% (26).

Nos EUA e apesar do advento da antibioterapia, as taxas de mortalidade por pneumonia têm-se mantido relativamente constantes desde que o acesso à penicilina se tornou universal (28). Contudo, recentemente, neste país foi registada uma diminuição da mortalidade por PAC para valores inferiores a 20 óbitos por 100.000 habitantes, que se atribuiu à vacinação por rotina das crianças com vacinas pneumocócicas conjugadas e à maior transparência e divulgação pública do processo de cuidados e das taxas de readmissão e mortalidade (23).

Em Portugal, os dados disponíveis de letalidade intra-hospitalar são muito escassos e limitados a curtos períodos temporais. No principal estudo disponível e relativo ao período de 1998-2000, a letalidade intra-hospitalar dos adultos internados por PAC foi de 17,3%, aumentando para 21,5% nos internados com idade ≥65 anos (15).

Estes dados nacionais justificam, igualmente, a necessidade de uma melhor caracterização da situação atual e da sua evolução temporal, em resultado das alterações demográficas ocorridas no nosso país.

2.4. Custos Diretos dos Internamentos por PAC

O tratamento de doentes com PAC está associado a importantes custos diretos, indiretos e intangíveis no ambulatório e, sobretudo, a nível hospitalar. Na União Europeia e com informação anterior a 2012, os custos anuais da PAC foram estimados em 10 biliões de Euros, dos quais €5,7 biliões em internamentos hospitalares, €0,5 biliões em cuidados de ambulatório, €0,2 biliões em fármacos e €3,6 biliões em custos indiretos pela perda de dias de trabalho (8,27).

Todos os estudos disponíveis apontam para a enorme diferença entre os custos dos doentes tratados em ambulatório e em regime hospitalar, independente da região ou população estudada. Por exemplo, em Espanha num estudo publicado em 2004, a média dos custos diretos dos doentes tratados em ambulatório foi de €196 contra um custo direto médio de €1.553 em internamento (29), um acréscimo de custo quase 8 vezes superior. Na Alemanha, num estudo publicado em 2005, a média dos custos diretos por internamento foi de €1.201 (30) e na Itália o custo médio dos cuidados de saúde por doente, incluindo um período de seguimento de 6 meses, foi de €1.586 (31).

Na análise dos custos diretos dos internamentos hospitalares a duração dos dias do internamento é uma parcela muito significativa da despesa e que se correlaciona com a idade dos doentes internados (11). Nos EUA, num estudo histórico e pioneiro publicado em 1998, a média dos custos dos internamentos nos doentes com idades <65 e ≥65 foi de $6.042 e $7.166, respetivamente (32). Em Espanha num estudo publicado em 2001, os custos com os doentes com idade ≥65 anos representavam 58% do total dos custos (33).

Em Portugal, e tanto quanto tenhamos conhecimento não existem estudos publicados e abrangentes com os custos dos internamentos de adultos por PAC. A existência de uma base de dados centralizada na ACSS com a informação clínica e administrativa das admissões hospitalares no SNS pode permitir uma melhor caracterização do

impacto económico da PAC e, em particular, dos custos diretos dos internamentos hospitalares.

2.5. Importância da prevenção da PAC

Os dados publicados e disponíveis para o nosso país e relativos ao período de 1998-2000 (15), justificam plenamente a importância de uma maior atenção à implementação de medidas de prevenção da PAC. Estas medidas no âmbito da promoção da saúde e da prevenção da doença incluem a intervenção em fatores de risco associados a estilos de vida e a vacinação contra a gripe e infeções pelo *Streptococcus pneumoniae*.

2.5.1. Fatores de risco associados a estilos de vida

Estão publicados vários estudos sobre o impacto da idade, comorbilidades e fatores de risco associados a estilos de vida no desenvolvimento de PAC (5,34). Nos dois principais estudos (5,34) são apresentadas as *Odds Ratio* (OR) associados ao risco de pneumonia.

No estudo publicado por Torres na revista *Thorax* em 2013 (34), destacam-se o tabagismo ativo (OR: 1,37 a 1,81), consumo de álcool >41 g/dia (OR: 1,59) e >80 g/dia (OR: 2,34), baixo peso ponderal (OR: 1,04 a 2,20), contato regular com crianças (OR: 1,48), e várias comorbilidades, das quais, DPOC (OR: 2,17 a 3,92), doença cardiovascular crónica (OR: 1,4 a 3,2), diabetes *mellitus* (OR: 1,43 a 1,54), doença hepática crónica (OR: 1,67 a 2,24) e doença renal crónica (OR: 1,7 a 2,15). A higiene oral com visita ao dentista/higienista está associada a um efeito protetor (OR: 0,59 a 0,71).

Estes valores de risco corroboram a necessidade de uma intervenção nos fatores de risco associados a estilos de vida e, em particular, no tabagismo e alcoolismo. De igual modo, os doentes com comorbilidades devem procurar evitar as exacerbações e, consequentemente, a progressão da doença. Por exemplo, nos doentes com DPOC, a gravidade da obstrução das vias aéreas está associada ao risco de incidência da PAC (7).

2.5.2. Vacinação contra a gripe e infeções a *Streptococcus pneumoniae*

O vírus influenza é o vírus mais importante e mais grave das infeções respiratórias inferiores, incluindo PAC (35), e *Streptococcus pneumoniae* é o mais frequente e importante patógeno da PAC (27). Estudos em animais sugerem um sinergismo

clinicamente relevante entre estes dois microrganismos, para os quais estão disponíveis vacinas (35).

A vacinação contra a gripe necessita de ser repetida anualmente em resultado do acumular de mutações nos vírus influenza circulantes que tornam ineficaz a vacina de um ano noutros anos. A RNA polimerase viral não tem mecanismos de correção de erros e os vírus influenza, particularmente do tipo A, têm uma taxa de mutação 300 vezes superior à dos outros microrganismos (35). A acumulação de mutações pontuais resulta num *drift* antigénico que permite ao vírus não ser reconhecido pela resposta imunitária adquirida nos anos anteriores (35).

O interesse da vacinação antigripal na prevenção da PAC está documentado em metaanálises, com predomínio de estudos observacionais, que quantificaram numa população de idosos residentes em lares vacinados com a vacina inativada trivalente, idêntica à vacina disponível no nosso país, uma diminuição significativa da pneumonia entre 53% (36) e 46% (37).

Estão comercializadas duas vacinas pneumocócicas, a vacina pneumocócica conjugada 13 valente (VPC13) e a vacina pneumocócica polisacarídica 23 valente (VPP23). As duas vacinas partilham 12 serotipos e, no total, cobrem 24 dos 97 serotipos de *Streptococcus pneumoniae* descritos até à presente data.

A inclusão da VPC13 nos planos nacionais de vacinação teve um impacto significativo na redução da incidência de doença invasiva pneumocócica nas crianças vacinadas, mas de igual modo na população adulta não vacinada, nomeadamente nos pais e avós das crianças (38). Esta proteção de grupo está igualmente documentada em estudos epidemiológicos. Nestes estudos e na sequência da vacinação generalizada de crianças com VPC13, verificou-se uma redução em 94% das infeções pneumocócicas invasivas pelos 13 serotipos vacinais em 94% em todos os grupos etários e uma quase erradicação nas crianças (38,39).

Um estudo controlado, aleatorizado e de referência a nível mundial, realizado na Holanda entre 2008 e 2010 (estudo CAPITA), com 84.496 adultos de idade ≥65 anos revelou uma eficácia da VPC13 de 45,6% na prevenção do 1º episódio de PAC e de 75,0% na doença invasiva pneumocócica, pelos serotipos vacinais (40).

Mais recentemente, num estudo em condições de "mundo real" realizado nos EUA entre 2015 e 2016 e envolvendo indivíduos com idade ≥65 anos, com uma média de idades de 76 anos e dos quais 87,9% com condições de risco ou de risco elevado para doença

invasiva pneumocócica, a PCV13 apresentou uma efetividade entre 71,1 e 73,3% na prevenção de PAC pelos serotipos vacinais (41).

Em relação à VPC13, a VPP23 só protege contra as formas invasivas de doença pneumocócica (35), não confere proteção de grupo (35) mas tem a vantagem de alargar a cobertura de serotipos (35).

Em Portugal, a vacinação contra a gripe e as infeções por *Streptococcus pneumoniae* estão abrangidas nas políticas de prevenção da doença da DGS. Para a gripe, a DGS emite uma Orientação de vacinação, atualizada anualmente e correspondendo a última à Orientação 018/2017 de 26/09/2017. Para as infeções pneumocócicas, a DGS emitiu a Norma 011/2015 de 23/06/2015 e atualizada a 06/11/2015, de vacinação contra infeções por *Streptococcus pneumoniae* de grupos com risco acrescido para doença invasiva pneumocócica. A norma contra a infeção por *Streptococcus pneumoniae* representa um marco na vacinação em Portugal com a mudança progressiva do paradigma da vacinação pediátrica para a imunização ao longo da vida.

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3. Finalidade e Objetivos

A finalidade desta tese de doutoramento é contribuir para um melhor conhecimento e caracterização do impacto dos internamentos de adultos por PAC em Portugal continental. E, com base nesses resultados, fundamentar a qualidade da decisão de internamento hospitalar e as medidas de intervenção nos fatores de risco associados a estilos de vida e de vacinação contra a gripe e as infeções pelo *Streptococcus pneumoniae*.

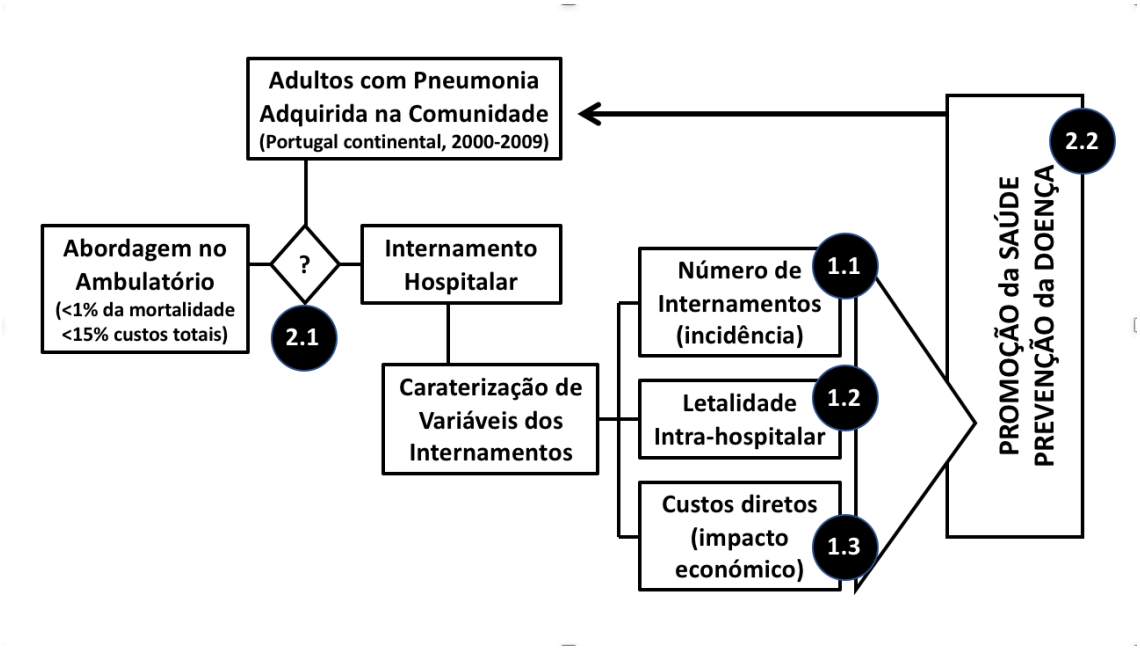

Figura 2 – Esquema conceptual da tese com identificação dos objetivos principais (1.1; 1.2; 1.3) e secundários (2.1; 2.2).

Para responder à pergunta de investigação, identificaram-se objetivos principais e secundários. Os objetivos principais são os seguintes:

3.1.Incidência dos internamentos de adultos por PAC em Portugal continental

Caracterização da incidência dos internamentos hospitalares por ano, género e grupo etário na população adulta residente em Portugal continental, no período de 2000 a 2009. Caracterização da evolução temporal no mesmo período.

Quantificação do número de internamentos por unidade de tempo (minutos).

Para responder a este objetivo apresentam-se os seguintes estudos:

1. *Hospital admissions of adults with community-acquired pneumonia in Portugal between 2000 and 2009*

   Autores: Filipe Froes, António Diniz, Margarida Mesquita, Margarida Serrado, Baltazar Nunes

   Ano de Publicação: 2013

   Revista: European Respiratory Journal 2013; 41: 1141–1146

   Fator de Impacto da revista: 7.125 (2013)

   Número de citações do artigo a 30/06/2018: 25

2. *Morbilidade e Mortalidade da Pneumonia Adquirida na Comunidade no Adulto, em Portugal*

   Autor: Filipe Froes

   Ano de Publicação: 2013

   Revista: Acta Médica Portuguesa 2013;26(6):644-645

   Fator de Impacto da revista: 0.281 (2013)

   Número de citações do artigo a 30/06/2018: 5

3.2. Letalidade intra-hospitalar dos internamentos de adultos por PAC em Portugal continental

Caracterização da letalidade intra-hospitalar dos internamentos hospitalares por ano, género e grupo etário na população adulta residente em Portugal continental, no período de 2000 a 2009. Caracterização da evolução temporal no mesmo período.

Quantificação do número óbitos por unidade de tempo (minutos).

Para responder a este objetivo apresentam-se os seguintes estudos:

3. *Intra-hospital mortality for Community-Acquired Pneumonia in mainland Portugal between 2000 and 2009*

   Autores: Francisca Teixeira Lopes, Ana Cysneiros, Ana Dias, Vera Durão, Fernanda Paula, Margarida Serrado, Baltazar Nunes, António Diniz, Filipe Froes

   Ano de Publicação: 2018

   Revista: Revista Portuguesa de Pneumologia

   Fator de Impacto da revista: 1.560 (2016)

Número de citações: 0 (aceite para publicação a 02/06/2018)

2. *Morbilidade e Mortalidade da Pneumonia Adquirida na Comunidade no Adulto, em Portugal*

   Autor: Filipe Froes

   Ano de Publicação: 2013

   Revista: Acta Médica Portuguesa 2013;26(6):644-645

   Fator de Impacto da revista: 0.281 (2013)

   Número de citações do artigo a 30/06/2018: 5

3.3. Custos diretos dos internamentos de adultos por PAC em Portugal continental

Caracterização dos custos diretos dos internamentos hospitalares globais no período de 2000 a 2009 e média de custos diretos por dia, por internamento e por resultado (vivo ou falecido).

Caraterização do período de tempo necessário para se gastar 1 Milhão de euros em custos diretos por internamentos hospitalares de adultos por PAC em Portugal continental.

Para responder a este objetivo apresenta-se o seguinte estudo:

4. *Direct Costs Related to the Admissions of Adults with Community Acquired Pneumonia in Mainland Portugal during the 2000-2009 Period*

   Autores: Filipe Froes, António Diniz, Patrícia Barbosa, Vera Durão, Francisca Teixeira Lopes, Ana Cysneiros, Ana Dias, Margarida Serrado, Cristina Bárbara, Ana Escoval

   Ano de Publicação: 2017

   Revista: American Journal of Respiratory and Critical Care Medicine 2017; Volume: 195; Pages A3927

   Fator de Impacto da revista: 13.204 (2016)

   Número de citações a 30/06/2018: 0

Em face da previsível dimensão das variáveis englobadas no objetivo principal do estudo, identificam-se os seguintes objetivos secundários:

3.4. Papel dos médicos na decisão crítica de internamento hospitalar por PAC

Para analisar esta questão, apresenta-se o seguinte artigo no formato de editorial:

5. *PSI, CURB-65, SMART-COP or SCAP? And the winner is... SMART DOCTORS*

   Autor: Filipe Froes

   Ano de Publicação: 2013

   Revista: Revista Portuguesa de Pneumologia 2013;19(6): 243-244

   Fator de Impacto da revista: 0.855 (2013)

   Número de citações do artigo a 30/06/2018: 7

3.5. Importância das medidas de promoção da saúde e de prevenção da doença na redução do impacto dos internamentos de adultos por PAC em Portugal continental

Na análise da importância das medidas de promoção de saúde e de prevenção da doença na redução do impacto dos internamentos hospitalares de adultos por PAC em Portugal continental, apresentam-se três artigos no âmbito da atuação nos fatores de risco associados a estilos de vida e da vacinação contra a gripe e antipneumocócica:

6. *Achoo, achis, ATCHIN! Vaccine you…*

   Autores: Filipe Froes, Francesco Blasi, Antoni Torres

   Ano de Publicação: 2018

   Revista: European Respiratory Journal 2018; 51(3):1702558

   Fator de Impacto da revista: 10.569 (2016)

   Número de citações do artigo a 30/06/2018: 1

7. *Consensus document for the prevention of respiratory infections in adults*

   Autores: Filipe Froes, António Diniz, Carlos Robalo Cordeiro, Margarida Serrado, António Ramalho de Almeida

   Ano de publicação: 2014

   Revista: Revista Portuguesa de Pneumologia 2014;20(2):111-114

Fator de Impacto da revista: 0.855 (2013)

Número de citações do artigo a 30/06/2018: 11

8. *Pneumococcal vaccination and chronic respiratory diseases*

   Autores: Filipe Froes, Nicolas Roche, Francesco Blasi

   Ano de Publicação: 2017

   Revista: International Journal of Chronic Obstructive Pulmonary Disease 2017;12, 3457

   Fator de Impacto: 3.157 (2016-2017)

   Número de citações a 30/06/2018: 1

Em conclusão, na resposta à pergunta de investigação, identificámos três objetivos principais (1.1, 1.2 e 1.3) e dois objetivos secundários (2.1 e 2.2). Apresentam-se um total de 8 artigos para analisar e caraterizar as respostas aos objetivos principais e secundários (tabela I).

Nº	Título do artigo	Revista	Fator impacto	N.º Citações (<30/06/2018)
1	Hospital admissions of adults with community-acquired pneumonia in Portugal between 2000 and 2009	European Respiratory Journal 2013; 41: 1141–1146	7.125	25
2	Morbilidade e Mortalidade da Pneumonia Adquirida na Comunidade no Adulto, em Portugal	Acta Médica Portuguesa 2013;26(6):644-645	0.281	5
3	Intra-hospital mortality for Community-Acquired Pneumonia in mainland Portugal between 2000 and 2009	Revista Portuguesa de Pneumologia (aceite para publicação em 02/06/2018)	1.560	-
4	Direct Costs Related to the Admissions of Adults with Community Acquired Pneumonia in Mainland Portugal during the 2000-2009 Period	American Journal of Respiratory and Critical Care Medicine 2017; 195: A3927	13.204	0
5	PSI, CURB-65, SMART-COP or SCAP? And the winner is... SMART DOCTORS	Revista Port Pneumologia 2013;19(6): 243-244	0.855	7
6	Achoo, achis, ATCHIN! Vaccine you…	European Respir Journal 2018; 51(3):1702558	10.569	1
7	Consensus document for the prevention of respiratory infections in adults	Revista Portuguesa de Pneumologia 2014;20(2):111-114	0.855	11
8	Pneumococcal vaccination and chronic respiratory diseases	Intern Journal of Chronic Obstructive Pulmonary Disease 2017;12, 3457	3.157	1

Tabela I – Artigos publicados com o título, revista, fator de impacto à data de publicação e número de citações a 30/06/2018.

4. Métodos

Os resultados desta tese consistem na publicação de 8 artigos em revistas indexadas, com *peer-review* e fator de impacto. Para responder aos objetivos principais e secundários da pergunta de investigação, apresenta-se de seguida a metodologia dos 8 estudos publicados (tabela II).

Objetivos principais	Nº artigo	Título do artigo	Tipo de artigo
1.1. Incidência dos internamentos de adultos por PAC em Portugal continental	1	Hospital admissions of adults with community-acquired pneumonia in Portugal between 2000 and 2009	Retrospetivo
	2	Morbilidade e Mortalidade da Pneumonia Adquirida na Comunidade no Adulto, em Portugal	Revisão
1.2. Letalidade intra-hospitalar dos internamentos de adultos por PAC em Portugal continental	3	Intra-hospital mortality for Community-Acquired Pneumonia in mainland Portugal between 2000 and 2009	Retrospetivo
	2	Morbilidade e Mortalidade da Pneumonia Adquirida na Comunidade no Adulto, em Portugal	Revisão
1.3. Custos diretos dos internamentos de adultos por PAC em Portugal continental.	4	Direct Costs Related to the Admissions of Adults with Community Acquired Pneumonia in Mainland Portugal during the 2000-2009 Period	Retrospetivo
Objetivos secundários	**Nº artigo**	**Título do artigo**	**Tipo de artigo**
2.1. Papel dos médicos da decisão crítica de internamento hospitalar por PAC	5	PSI, CURB-65, SMART-COP or SCAP? And the winner is... SMART DOCTORS	Artigo de opinião / Editorial
2.2. Importância das medidas de promoção da saúde e de prevenção da doença na redução do impacto dos internamentos de adultos por PAC em Portugal continental	6	Achoo, achis, ATCHIN! Vaccine you…	Artigo de opinião / Editorial
	7	Consensus document for the prevention of respiratory infections in adults	Documento de consenso (Sociedade Portuguesa de Pneumologia)
	8	Pneumococcal vaccination and chronic respiratory diseases	Revisão

Tabela II – Objetivos principais e secundários e respetivos artigos publicados.

4.1. Objetivos principais

4.1.1. Incidência dos internamentos de adultos por PAC em Portugal continental

1. *Hospital admissions of adults with community-acquired pneumonia in Portugal between 2000 and 2009*

   Autores: Filipe Froes, António Diniz, Margarida Mesquita, Margarida Serrado, Baltazar Nunes

   Revista: European Respiratory Journal 2013; 41: 1141–1146

   Tipo de estudo: retrospetivo com análise estatística descritiva

   Período analisado: 2000 a 2009

   Metodologia:

   Análise da base de dados da ACSS, do Ministério de Saúde, que contém os dados administrativos e clínicos de todas as admissões nos hospitais do SNS, que abrange quase toda a população residente em Portugal continental no período analisado. A informação clínica, incluindo os diagnósticos e os procedimentos, é codificada a partir das notas de alta dos internamentos hospitalares por médicos com formação específica, utilizando a ICD-9-CM.

   Neste estudo, foram analisados retrospetivamente os internamentos hospitalares de adultos com o diagnóstico principal de pneumonia (ICD9: 480 a 486 e 487.0), que tiveram alta nos anos de 2000 a 2009. Os códigos utilizados excluem as formas de pneumonia tuberculosa ou pneumonia obstrutiva associada, por exemplo, a neoplasia do pulmão. Excluíram-se ainda os doentes menores de 18 anos e os doentes com pneumonia como diagnóstico não principal. Como a ICD-9-CM não especifica se a pneumonia é adquirida na comunidade, excluíram-se também os doentes infetados com o VIH (ICD9: 042 a 044 e GDH: 488, 489 e 490), imunocomprometidos por antineoplásicos ou imunossupressores (causa externa de doença: código E933.1) e transplantados (V42). Na análise da informação clínica foi assegurado o anonimato dos doentes.

   No que respeita à dimensão da população, utilizaram-se as estimativas de população residente em Portugal Continental para o final do respetivo ano, subdivididas por grupos etários e género, para cada um dos anos em estudo, extraídas do Infoline do Instituto Nacional de Estatística (www.ine.pt).

Para produção dos indicadores de interesse para este estudo procedeu-se a uma análise estatística descritiva, tendo-se calculado: taxas de internamento por PAC por 1.000 habitantes, percentagem de internamentos por PAC no total de internamentos por todos os diagnósticos, distribuição proporcional dos internamentos por PAC por grupo etário e sexo e, por fim, médias e medianas da idade dos internados por PAC.

Todos os cálculos apresentados foram obtidos com base no pacote de programas estatísticos STATA SE 11 (StataCorp. 2009. Stata Statistical Software: Release 11. College Station, TX: StataCorp LP) e a folha de cálculo Microsoft Excel® (Microsoft Corp., Redmond, WA, USA).

2. *Morbilidade e Mortalidade da Pneumonia Adquirida na Comunidade no Adulto, em Portugal*

   Autor: Filipe Froes

   Revista: Acta Médica Portuguesa 2013;26(6):644-645

   Tipo de estudo: artigo de revisão

   Período analisado: N/A

   Metodologia:

   Artigo de revisão com análise comparativa dos dados nacionais (estudo n.º 1) com dados de incidência de PAC e de internamentos hospitalares internacionais, com destaque noutros países europeus.

4.1.2. Letalidade intra-hospitalar dos internamentos de adultos por PAC em Portugal continental

3. *Intra-hospital mortality for Community-Acquired Pneumonia in mainland Portugal between 2000 and 2009*

   Autores: Francisca Teixeira Lopes, Ana Cysneiros, Ana Dias, Vera Durão, Fernanda Paula, Margarida Serrado, Baltazar Nunes, António Diniz, Filipe Froes

   Revista: Revista Portuguesa de Pneumologia (aceite para publicação a 02/06/2018)

   Tipo de estudo: retrospetivo com análise estatística descritiva

   Período analisado: 2000 a 2009

Metodologia:

Análise da base de dados ACSS, do Ministério de Saúde, que contém os dados administrativos e clínicos de todas as admissões nos hospitais do SNS, que abrange quase toda a população residente em Portugal continental no período analisado. A informação clínica, incluindo os diagnósticos e os procedimentos, é codificada a partir das notas de alta dos internamentos hospitalares por médicos com formação específica, utilizando a ICD-9-CM.

Neste estudo, foram selecionados retrospetivamente todos os internamentos com o diagnóstico principal de pneumonia (ICD9: 480 a 486 e 487.0), no período compreendido entre 2000 a 2009 e dentro destes analisados os casos de morte intra-hospitalar, independentemente da duração do internamento. Os códigos utilizados excluem as formas de pneumonia tuberculosa ou pneumonia obstrutiva associada, por exemplo, a neoplasia do pulmão. Excluíram-se, ainda, os doentes menores de 18 anos e os doentes com pneumonia como diagnóstico não principal. Como a ICD-9-CM não especifica se a pneumonia é adquirida na comunidade, excluíram-se também os doentes infetados com o VIH (ICD9: 042 a 044 e GDH: 488, 489 e 490), imunocomprometidos por antineoplásicos ou imunossupressores (causa externa de doença: código E933.1) e transplantados (V42). Na análise da informação clínica foi assegurado o anonimato dos doentes.

A comparação entre as médias de idade dos grupos foi efetuada usando o teste T de Student ou Mann-Whitney caso os pressupostos do primeiro teste não se verificassem. O risco de morrer foi comparado entre grupos etários, sexos e ano utilizando o teste de Qui-quadrado. Calcularam-se também os riscos relativos de morte intra-hospitalar nas várias categorias das variáveis em estudo e seus respetivos intervalos a 95% de confiança. Para medir a associação de cada variável (ano, grupo etário e sexo) no risco de morte ajustado para as outras variáveis aplicou-se um modelo de regressão log-binomial. O nível de significância considerado para todos os testes efetuados foi 5%. Todos os cálculos apresentados foram obtidos com os pacotes de programas estatísticos SPSS 20 e STATA SE 11.

4. *Morbilidade e Mortalidade da Pneumonia Adquirida na Comunidade no Adulto, em Portugal*

   Autor: Filipe Froes

   Revista: Acta Médica Portuguesa 2013;26(6):644-645

Tipo de estudo: artigo de revisão

Período analisado: N/A

Metodologia:

Artigo de revisão com análise comparativa dos dados nacionais (estudo n.º 3) com dados internacionais de mortalidade e letalidade intra-hospitalar dos internamentos hospitalares de adultos por PAC, com destaque noutros países europeus.

4.1.3. Custos diretos dos internamentos de adultos por PAC em Portugal continental

5. *Direct Costs Related to the Admissions of Adults with Community Acquired Pneumonia in Mainland Portugal during the 2000-2009 Period*

   Revista: American Journal of Respiratory and Critical Care Medicine 2017; Volume: 195; Pages A3927 (apresentação de poster)

   Tipo de estudo: retrospetivo com análise estatística descritiva

   Período analisado: 2000 a 2009

   Metodologia:

   Análise retrospetiva da base de dados da ACSS, de todas as admissões hospitalares no SNS. Inclusão dos internamentos de adultos com o diagnóstico principal de pneumonia (ICD-9-CM 480-486 e 487.0) no período de 2000 a 2009. Exclusão dos doentes com idade inferior a 18 anos, os internamentos em que a pneumonia não era o diagnóstico principal, os doentes com infeção VIH (ICD9:042-044 e/ou GDH 488, 489 ou 490), os doentes imunocomprometidos por terapêuticas antineoplásicas ou imunossupressoras (Código E933.1 – causa externa de doença) e os doentes transplantados (V42). Foi assegurada a anonimidade dos dados dos doentes.

   De acordo com a portaria dos Grupos de Diagnóstico Homogéneo (GDH) foi calculado o custo direto do internamento de acordo com os valores estabelecidos para o respetivo ano do internamento. Determinaram-se, assim, os custos diretos dos internamentos por ano, dia e de acordo com o resultado à alta (vivo ou falecido), com recurso à folha de cálculo Microsoft Excel® (Microsoft Corp., Redmond, WA, USA).

Estes dados foram apresentados em póster na conferência anual da *American Thoracic Society*, em Washington, de 19 a 24 de maio de 2017.

4.2. Objetivos secundários

4.2.1. Papel dos médicos na decisão crítica de internamento hospitalar por PAC

6. *PSI, CURB-65, SMART-COP or SCAP? And the winner is... SMART DOCTORS*

   Autor: Filipe Froes

   Revista: Revista Portuguesa de Pneumologia 2013;19(6): 243-244

   Tipo de estudo: artigo de opinião/editorial

   Período analisado: N/A

   Metodologia:

   Artigo de opinião, publicado como editorial na Revista Portuguesa de Pneumologia.

4.2.2. Importância das medidas de promoção da saúde e de prevenção da doença na redução do impacto dos internamentos de adultos por PAC em Portugal continental

7. *Achoo, achis, ATCHIN! Vaccine you…*

   Autores: Filipe Froes, Francesco Blasi, Antoni Torres

   Revista: European Respiratory Journal 2018; 51(3):1702558

   Tipo de estudo: artigo de opinião/editorial

   Período analisado: N/A

   Metodologia:

   Artigo de opinião, publicado como editorial no European Respiratory Journal. Um dos coautores, Francesco Blasi, foi presidente da *European Respiratory Society* em 2012-2013.

8. *Consensus document for the prevention of respiratory infections in adults.*

   Autores: Filipe Froes, António Diniz, Carlos Robalo Cordeiro, Margarida Serrado, António Ramalho de Almeida

   Revista: Revista Portuguesa de Pneumologia 2014;20(2):111-114

Tipo de artigo: documento de consenso

Período analisado: N/A

Metodologia:

Documento de consenso da Sociedade Portuguesa de Pneumologia. Procedeu-se a uma extensa revisão da evidência disponível para fundamentar medidas de intervenção geral e vacinação antigripal e antipneumocócica.

9. *Pneumococcal vaccination and chronic respiratory diseases*

Autores: Filipe Froes, Nicolas Roche, Francesco Blasi

Revista: International Journal of Chronic Obstructive Pulmonary Disease 2017;12, 3457

Tipo de artigo: artigo de revisão

Período analisado: N/A

Metodologia:

Artigo de revisão da literatura sobre o impacto da vacinação antipneumocócica na prevenção de exacerbações e episódios de pneumonia numa população particularmente vulnerável, os doentes com DPOC.

5. Resultados

Apresentam-se os 8 artigos publicados com os resultados e que se discriminam na tabela III.

Nº	Título do artigo	Revista	Autores
1	Hospital admissions of adults with community-acquired pneumonia in Portugal between 2000 and 2009	European Respiratory Journal 2013; 41: 1141–1146	Filipe Froes, António Diniz, Margarida Mesquita, Margarida Serrado, Baltazar Nunes
2	Morbilidade e Mortalidade da Pneumonia Adquirida na Comunidade no Adulto, em Portugal	Acta Médica Portuguesa 2013;26(6):644-645	Filipe Froes
3	Intra-hospital mortality for Community-Acquired Pneumonia in mainland Portugal between 2000 and 2009	Revista Portuguesa de Pneumologia (aceite para publicação em 02/06/2018)	Francisca T Lopes, Ana Cysneiros, Ana Dias, Vera Durão, Fernanda Paula, Margarida Serrado, Baltazar Nunes, António Diniz, Filipe Froes
4	Direct Costs Related to the Admissions of Adults with Community Acquired Pneumonia in Mainland Portugal during the 2000-2009 Period	American Journal of Respiratory and Critical Care Medicine 2017; 195: A3927	Filipe Froes, António Diniz, Patrícia Barbosa, Vera Durão, Francisca Teixeira Lopes, Ana Cysneiros, Ana Dias, Margarida Serrado, Cristina Bárbara, Ana Escoval
5	PSI, CURB-65, SMART-COP or SCAP? And the winner is... SMART DOCTORS	Revista Port Pneumologia 2013;19(6): 243-244	Filipe Froes
6	Achoo, achis, ATCHIN! Vaccine you…	European Respir Journal 2018; 51(3):1702558	Filipe Froes, Francesco Blasi, Antoni Torres
7	Consensus document for the prevention of respiratory infections in adults	Revista Portuguesa de Pneumologia 2014;20(2):111-114	Filipe Froes, António Diniz, Carlos Robalo Cordeiro, Margarida Serrado, António Ramalho de Almeida
8	Pneumococcal vaccination and chronic respiratory diseases	Intern Journal of Chronic Obstructive Pulmonary Disease 2017;12, 3457	Filipe Froes, Nicolas Roche, Francesco Blasi

Tabela III – Artigos publicados com o título, revista e autores.

5.1. Hospital admissions of adults with community-acquired pneumonia in Portugal between 2000 and 2009 (Artigo N.º 1)

Autores: Filipe Froes, António Diniz, Margarida Mesquita, Margarida Serrado, Baltazar Nunes

Ano de Publicação: 2013

Revista: European Respiratory Journal 2013; 41: 1141–1146

Fator de Impacto da revista: 7.125 (2013)

Número de citações do artigo a 30/06/2018: 25

Eur Respir J 2013; 41: 1141–1146
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Hospital admissions of adults with community-acquired pneumonia in Portugal between 2000 and 2009

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Hospital admissions of adults with community-acquired pneumonia in Portugal between 2000 and 2009

Filipe Froes*, António Diniz*, Margarida Mesquita#, Margarida Serrado* and Baltazar Nunes¶

ABSTRACT: Recent studies in the USA and northern Europe have shown an increase in community-acquired pneumonia (CAP). In southern Europe, this increase has not yet been documented.

We carried out a retrospective analysis from encoded information from the Portuguese database for hospital admissions that included all individuals aged ⩾18 years, with a primary diagnosis of pneumonia, who were discharged between 2000 and 2009. We excluded patients infected with HIV, individuals immunocompromised as a result of anti-cancer or immunosuppressive treatment, and transplant recipients.

Of the 294 027 admissions for CAP, 56% were male. The mean age was 73.1 years and the median age 77 years. Between 2000 and 2009, there was a 5% increase in the average age of patients admitted with CAP.

Admissions for CAP represented 3.7% of total admissions of adult patients. The average annual rate of hospital admissions for adults with CAP was 3.61 per 1000 total population, rising to 13.4 for those aged ⩾65 years. Between 2000–2004 and 2005–2009 the average annual rate of hospital admission for CAP per 1000 population increased by 28.2%.

Hospital admissions for CAP in Portugal increased between 2000 and 2009. It has grown consistently over time, varying according to age with males over-represented.

KEYWORDS: Community-acquired pneumonia, incidence, pneumonia

Prospective studies prior to 1987 in the USA and in northern European countries estimated an annual rate of between five and 11 cases of community-acquired pneumonia (CAP) per 1000 adult population [1–3].

The percentage of adults having to be hospitalised with CAP was very variable. Depending on the country or region analysed, the length of the study and the period in which it took place, there were differences in the population studied and the organisation of the health systems, in addition to climatic variation and the annual and seasonal changes of circulating microorganisms (*e.g. Mycoplasma pneumoniae* and respiratory virus).

Data published in the USA and Canada before 2000 documented global annual rates of adult hospital admissions with CAP of between 1.1 and four cases per 1000 inhabitants [4, 5], which increased to 13.2 cases per 1000 inhabitants among those aged >55 years [6]. In the USA [7] and the countries of northern Europe, such as the UK [8], Denmark [9] and the Netherlands [10], recent studies have shown a steady increase in the number of hospital admissions for pneumonia. In the UK, between 1997–1998 and 2004–2005, there was an increase of 34% in the annual average rate of admission of patients with a primary diagnosis of pneumonia [8].

In Portugal, a southern European country, data relating to 1998–2000 show that adult admission with CAP was 2.9% of the total hospital admissions for all causes [11]. During this period, there was an average annual rate of hospitalisation of 2.66 per 1000 population ⩾15 years of age and 9.78 per 1000 for the group aged ⩾65 years. The average age for patient admission was 69.8 years [11]. This study aims to characterise the incidence of adult admission with CAP between the years 2000 and 2009, and to analyse its evolution over these 10 years.

METHODS

The Central Administration of the Health System of the Portuguese Ministry of Health contains administrative and clinical data of all admissions

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to National Health hospitals, which covers almost the whole resident population of mainland Portugal. The clinical information, including diagnoses and procedures, is encoded from the details of the hospital discharge report by medical staff who have been specially trained in hospital coding, using the International Classification of Diseases, 9th Revision Clinical Modification (ICD-9-CM) [12].

In this study, we analysed retrospectively the hospital admissions of adults with a primary discharge diagnosis of pneumonia (ICD-9-CM 480–486 and 487.0) who were discharged between 2000 and 2009. Patients under 18 years of age and those in whom pneumonia was not the main diagnosis were excluded. As ICD-9-CM does not specify whether pneumonia is community acquired, we also excluded patients with HIV (ICD-9-CM 042–044 and/or diagnosis-related groups 488, 489 and 490), individuals who were immunocompromised by anti-cancer or immunosuppressive treatment (external cause of disease code E933.1) and transplant recipients (V42). The analysis of clinical information maintained patient anonymity.

The size of the population of mainland Portugal was obtained from the information line of the National Institute of Statistics [13] and corresponds to the estimates of the resident population at the end of the year, subdivided by age and sex, for each year of the study.

To obtain the relevant indicators for this study, we adopted a descriptive statistical analysis approach having calculated the following: Rates of admission for CAP per 1000 population, percentage of admissions for CAP from total admissions for all diagnoses, proportional distribution of admissions by age group and sex and, finally, average and median ages of CAP admissions.

All the calculations presented were obtained using the statistical software package STATA (release 11; StataCorp, College Station, TX, USA) and the Microsoft Excel spreadsheet (Microsoft Corp., Redmond, WA, USA).

RESULTS

Patient characteristics

A total of 294 027 admissions for CAP were included in the study for the 10-year period between 2000 and 2009. Of this total, 56% were males and 44% females. The median age was 77 years and the mean±SD age was 73.1±16.0 years, with a median age of 75 years and mean±SD age of 71.3±15.9 years for males and a median age of 79 years and an mean±SD age of 75.3±15.7 years for females. The greatest age was 109 years for females and 111 years for males. During the course of the study, we observed a consistent increase in the annual average age of patients of both sexes (fig. 1).

In the older patient age groups, aged 75–84 and ⩾85 years, there was an increase in the average age. From 2000 to 2009, the average age increased by 0.45 and 0.46 years for patients aged 75–84 and ⩾85 years, respectively.

Out of a total 294 027 patients studied, 10.3% were between 18 and 49 years of age, 11.9% between 50 and 64 years, 19.5% between 65 and 74 years, 34.7% between 75 and 84 years, and 23.6% aged ⩾85 years.

Admissions for CAP per total admissions

In mainland Portugal, between 2000 and 2009, a total of 7 849 266 hospital admissions occurred. Of this total, 294 027 (3.7%) were diagnosed with pneumonia and, according to the criteria for inclusion of this study, were considered to have CAP. The proportion of CAP admissions was greater in the older age groups, constituting 5.5% of those aged ⩾50 years, 7.0% of those aged ⩾65 years, 9.4% of those aged ⩾75 years and 13.8% of those aged ⩾85 years. For patients under the ages of 50 and 65 years, the percentages of admissions for CAP were 1.0% and 1.4%, respectively.

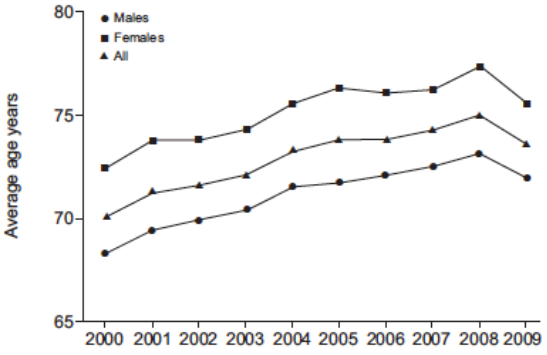
Between the periods 2000–2004 and 2005–2009 there was an increased rate of admission for CAP in all age groups; this was independent of sex but more marked in patients aged >65 years (table 1).

Throughout the 10 years of the study, we observed an increase in the percentage of admissions for CAP in the total admissions; this was particularly marked in the older age groups (fig. 2).

Incidence of admissions for CAP per 1000 total population

Between 2000 and 2009, there was an average annual incidence of 3.61 admissions of adults with CAP per 1000 population. Between the age groups of <50 and ⩾50 years the incidence increased from 0.66 to 7.49. In the age groups <65 and ⩾65 years, the incidence increased from 1.02 to 13.40. From 2000 to 2009, the incidence of admission per 1000 population went up 55.6%, from 3.02 to 4.70 and, in the 5-year periods 2000–2004 and 2005–2009, it increased by 28.2%. With the exception of the 18–29-year-old subjects, this increase was progressive year on year for all the other age groups (table 2).

If we exclude the year 2009 from the analysis, because of the influenza pandemic, we can see that the increase in hospital admissions per 1000 population during the periods 2000–2004 and 2005–2008 was 23.5%; this increase was observed only in the age groups aged ⩾50 years.



Age years										
Males	68.3	69.4	69.9	70.4	71.5	71.7	72.1	72.5	73.1	72.0
Females	72.4	73.8	73.8	74.3	75.5	76.3	76.1	76.2	77.3	75.5
All	70.1	71.3	71.6	72.1	73.3	73.8	73.8	74.2	75.0	73.6

FIGURE 1. Evolution of the average age of adult admissions for community-acquired pneumonia by sex and year between 2000 and 2009 in mainland Portugal.

TABLE 1 Percentage of admissions for community-acquired pneumonia from total adult admissions by sex and age group in the 5-year periods 2000–2004 and 2005–2009, and 2000–2009 in mainland Portugal

	Period	Age group years %						
		18–29	30–49	50–64	65–74	75–84	>85	Overall
Males	2000–2004	1.3	2.2	2.7	4.4	8.1	14.6	4.4
	2005–2009	1.5	2.4	2.9	4.9	9.6	17.3	5.4
	2000–2009	1.4	2.3	2.8	4.6	8.9	16.2	4.9
Females	2000–2004	0.3	0.6	1.6	3.2	5.9	11.0	2.5
	2005–2009	0.4	0.7	1.7	3.5	7.1	13.5	3.3
	2000–2009	0.4	0.6	1.7	3.3	6.6	12.5	2.9
Overall	2000–2004	0.6	1.2	2.2	3.8	7.0	12.3	3.3
	2005–2009	0.6	1.3	2.3	4.2	8.3	15.0	4.2
	2000–2009	0.6	1.2	2.3	4.0	7.7	13.8	3.7

The average global admission incidence for CAP was higher for males than females, at 4.21 and 3.07, respectively, per 1000 population (table 2). In those aged >50 years, this figure increased to 9.14 for males and 6.14 for females. For those aged >65 years, it grew to 16.73 for males and 10.64 for females.

Over the 10 years it can be observed that the annual increase in CAP admissions per 1000 population was most noticeable in the group aged ⩾75 years (fig. 3).

DISCUSSION

The Portuguese Ministry of Health database is essentially administrative. The clinical information is coded from discharge documents; this work is carried out exclusively by medical doctors who have been formally trained in hospital coding to make the process more rigorous. The Ministry of Health carries out regular audits, both internally and externally, of this coding process.

In this study, to exclude patients with complications from nosocomial pneumonia, only those cases with a primary discharge diagnosis of pneumonia were analysed. However, it is likely that some cases of nosocomial pneumonia may have been included due to coding error or because the database did not allow for the identification of patients re-admitted soon after a recent discharge from hospital. Patients living in nursing homes or in institutions for long-term care could not be identified from the database so it is likely that cases of pneumonia have been included that are healthcare related, particularly among the elderly. However, this concept and its inclusion in nosocomial pneumonia is not universally agreed on and for some authors would not be valid for Europe [14]. The fact that hospitalisation is more accessible and the reluctance to let patients die at home without support may explain the inclusion in the study of elderly patients with end-of-life pneumonia.

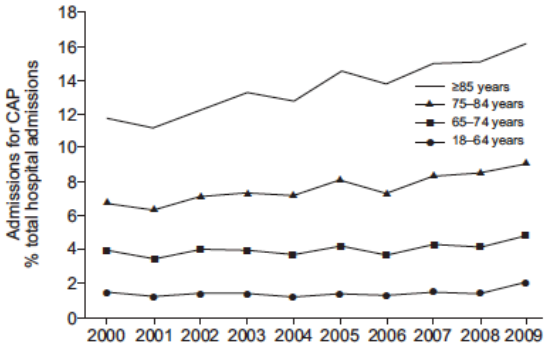


FIGURE 2. Evolution of the annual percentage of admissions for community-acquired pneumonia (CAP) out the total adult admissions by age group between 2000 and 2009 in mainland Portugal.

In this study, the information about the length of stay in hospital, which could have helped to make the methodology more specific, was not measured [15]. Likewise, there were no data available relating to the vaccination status of hospitalised patients, and it was also not possible to evaluate the impact of comorbidities in hospital admissions. The exclusion of patients infected with HIV, transplant recipients and those admitted for causes external to the disease, such as anticancer treatment or immunosuppressors, could have increased the accuracy of identification of admissions with CAP.

Apart from these limitations, the methodologies are similar to those that have been used in other countries [6, 8, 11, 16]. One advantage of this study is that it covers a period of 10 years, a fact that can minimise the impact of years that deviate from the norm, such as 2009 when the influenza pandemic H1N1 occurred. Official data in Portugal estimate that, in 2009 and 2010, 2400 patients were admitted to hospital as a result of the influenza pandemic A(H1N1) 2009 [17]. Our analysis does not cover the year 2010, and it was not possible to separate out the admissions due to the pandemic that occurred in 2009 from those that occurred in 2010 [17]. It is possible that hospital admissions for the A (H1N1) pandemic could represent up to 0.8% of the total admissions on our database and 6.2% of the admissions in 2009. We do not have information on the average age of patients admitted, but official data document that the 124 deaths caused by the pandemic correspond to a mortality rate of 1.17 deaths per 100 000 population, with an average age at death of 47.6 years [18]. According to these data,

TABLE 2 Incidence of admission for community-acquired pneumonia per 1000 adult population by age group and sex in the 5-year periods 2000–2004 and 2005–2009, and 2000–2009, and percentage variation during 5-year periods in mainland Portugal

	Period	Age years						
		18–29	30–49	50–64	65–74	75–84	>85	Overall
Males	2000–2004	0.45	1.05	2.53	7.70	20.83	46.61	3.72
	2005–2009	0.43	1.06	2.78	8.57	25.88	64.73	4.68
	2000–2009	0.44	1.06	2.66	8.14	23.53	56.33	4.21
Females	2000–2004	0.36	0.52	1.27	3.91	11.24	30.24	2.65
	2005–2009	0.36	0.58	1.36	4.31	13.77	41.69	3.47
	2000–2009	0.36	0.55	1.32	4.11	12.59	36.41	3.07
Overall	2000–2004	0.40	0.78	1.87	5.60	15.06	38.15	3.16
	2005–2009	0.39	0.82	2.04	6.22	18.59	49.25	4.05
	2000–2009	0.40	0.80	1.96	5.92	16.94	44.30	3.61
Variation 2000–2004 to 2005–2009 %		-2.5	+5.1	+9.1	+11.1	+23.4	+29.1	+28.2

it is possible that the influenza pandemic could have had an impact on the increased numbers of hospital admissions that occurred in 2009, particularly in the groups aged <50 years.

In the period from 2000 to 2009, the average age of patients admitted for CAP and the median age were, respectively, 73.1 and 77 years (71.3 and 75 years for males and 75.3 and 79 years for females). The reduction in the average age of patients admitted in 2009 (fig. 1) could have been related to the influenza pandemic. The age factor is patently clear: 89.7% of admissions were aged ⩾50 years, 77.8% were ⩾65 years, 58.3% were ⩾75 years and 23.6% were ⩾85 years.

These data are very similar to those that EWIG *et al.* [19] found in Germany between 2005 and 2006. In our study, we also confirmed the impact of age on the increase in admissions for CAP. The average age grew from 70.1 years in 2000 to 73.6 years in 2009, which corresponds to an increase of 5.0% in the average age over a decade. This increase is greater than the increase in average life expectancy in Portugal, which, between 2000 and 2009, changed from 73 to 76 years for males and from 80 to 82 years for females [20]. The half-year increase in the average age of the older patients, *i.e.* those aged between 75 and 84 years and ⩾85 years, between 2000 and 2009, could be one of the contributing factors to the increased numbers of admissions among these age groups.

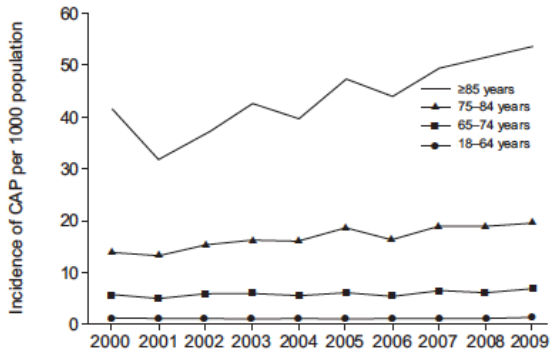


FIGURE 3. Evolution of the annual incidence of admission for community-acquired pneumonia (CAP) per 1000 population by age group between 2000 and 2009 in mainland Portugal.

As recorded in other recent publications [16, 19, 21] more males (56%) were admitted to hospital than females (44%); the percentages are similar to those in Germany [19].

Between 2000 and 2009, the total number of episodes of hospital admissions for all causes was relatively stable, varying by 3.3% between the two 5-year periods of 2000–2004 and 2005–2009. Admission for CAP represented 3.7% of all admissions. Between 2000 and 2004 (3.3%) and 2005 and 2009 (4.2%), there was an increase of 27.3%. In relation to the period 1998–2000, the increase was 27.6% [11]. These figures confirm the increase in admission for CAP in absolute and percentage numbers.

The increase in percentage of admissions for CAP is equally dependent on age, above all in those aged >65 years, of whom those aged ⩾75 years had the highest percentages. Admission for CAP for patients aged ⩾65 years is five times greater than for those aged <65 years.

For the 10 years of the study, the average annual incidence for hospital admissions for adults with CAP per 1000 population was 3.61. Analysis by age group appears to confirm the importance of age and sex. This value always increased with age, from 7.49 and 13.40 per 1000 population in the age groups ⩾50 and ⩾65 years, respectively, up to a maximum value of 44.30 for patients aged >85 years. In the same way, it can be seen that the incidence of admission for CAP per 1000 population for the age group ⩾65 years is 13 times greater than for the age group <65 years. The incidence of admissions was always greater for males than for females in all age groups.

In Portugal, the values for incidence of admission per 1000 population between 2000 and 2009 are much higher than those recorded in the period 1998 to 2000 [11]. These values are also

higher than those found in recent studies in other countries. In Germany, in 2005 and 2006, we found an average value of 2.86 admissions per 1000 adults [19]. In Spain, from 2003 to 2007, the values were 6.27 and 10.29 per 1000 population in the age groups ⩾50 years and ⩾65 years, respectively [16], as opposed to the 7.49 and 13.40 per 1000 population in our study. In England, in 2004–2005, the age-standardised incidence of hospital admissions with a primary diagnosis of pneumonia was 22.18 per 1000 population in the age group ⩾85 years [8]. Even allowing for differences in methodology, given the significant contrast with the figures for Portugal for the ⩾85 years age group (44.30 *versus* 22.18), the implication of these figures about the impact of pneumonias at end-of-life in our series must be investigated.

With the exception of the age group 18–29 years, in the rest of the age groups there has been a progressive increase in the incidence of admission for CAP per 1000 population between the 5-year periods of 2000–2004 and 2005–2009, with a global increase of 28.2%. If we exclude the year 2009 from our analysis, because of the influenza pandemic, the incidence of hospital admissions per 1000 population increased by 23.5% in the periods 2000–2004 and 2005–2008 and this increase is only in the groups aged ⩾50 years. Excluding the year 2009 confirms that the steady increase of admissions per 1000 population preceded the influenza pandemic and suggests that the pandemic had impacted on the increased of hospital admissions in the groups aged <50 years.

The percentage of increase of hospital admissions per 1000 population in Portugal is lower than that found in England (34% between 1997 and 1998 and between 2004 and 2005) in an age-standardised study that did not exclude patients who were immunocompromised and did include paediatric patients [8].

In Portugal, there has been a steady increase in the proportion of hospital admissions for CAP. This variation has been growing steadily over time, is increasing with age and is more marked among males. The study did not identify the causes of this increase nor explain the differences to other countries. These differences could be due to any or all of the following: an ageing population, increased comorbidities, greater ease of access to hospital services and inadequate implementation of preventive measures. In Portugal, the official data do not include information about pneumococcal vaccines and show that, in the periods from 1998 to 1999 and 2007 to 2008, the rate of coverage of the anti-flu vaccine in the population in general remained at 14.2–14.5%, but increased from 31.3% to 51.0% for people aged ⩾65 years [22].

We do not know whether this increase in the hospital context is matched by an increase in the incidence of the disease in outpatients. We conclude that now is the time to obtain a more accurate characterisation of patients hospitalised and also to re-evaluate the global incidence of pneumonia in the community.

SUPPORT STATEMENT

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STATEMENT OF INTEREST

None declared.

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5.2. Morbilidade e Mortalidade da Pneumonia Adquirida na Comunidade no Adulto, em Portugal
(Artigo N.º 2)

Autores: Filipe Froes

Ano de Publicação: 2013

Revista: Acta Médica Portuguesa 2013;26(6):644-645

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Morbilidade e Mortalidade da Pneumonia Adquirida na Comunidade no Adulto, em Portugal

Morbidity and Mortality of Community-Acquired Pneumonia in Adults, in Portugal

Filipe FROES[1,2,3]

Acta Med Port 2013 Nov-Dec;26(6):644-645

PERSPECTIVA

Morbilidade e Mortalidade da Pneumonia Adquirida na Comunidade no Adulto, em Portugal

Morbidity and Mortality of Community-Acquired Pneumonia in Adults, in Portugal

Filipe FROES[1,2,3]
Acta Med Port 2013 Nov-Dec;26(6):644-645

Palavras-chave: Infecções Comunitárias Adquiridas; Hospitalização; Pneumonia/mortalidade; Portugal.
Keywords: Community-Acquired Infections; Epidemiologic Factors; Hospitalization; Pneumonia/mortality; Portugal.

A pneumonia adquirida na comunidade (PAC) é uma causa importante de morbilidade, mortalidade e consumo de recursos de saúde na população adulta. A incidência aumenta com a idade e é maior nos homens do que nas mulheres.[1]

Na última década, estudos em diferentes países[2,3] documentaram um aumento do número de internamentos hospitalares por PAC. O aumento da esperança média de vida e, consequentemente, da população idosa, a par da crescente prevalência das doenças crónicas não-transmissíveis são alguns dos principais fatores que explicam esta situação.

O aumento dos internamentos por PAC também se verificou em Portugal.[4] Este aumento só foi possível documentar em Portugal continental por ausência de informação disponível relativa às Regiões Autónomas dos Açores e da Madeira. Assim, no período de 2000 a 2009, a pneumonia adquirida na comunidade foi uma das principais causas de internamento hospitalar no nosso país, representando 3,7% do total de episódios de internamento hospitalar de adultos por todas as causas em instituições do Serviço Nacional de Saúde.[4] Este valor aumentou com a idade, representando 7,0% nos indivíduos com idade ≥ 65 anos.[4] Neste período, foram internados mais homens do que mulheres, 56% e 44% respetivamente, e a média de idades dos doentes internados foi de 73 anos.[4] De destacar que 10% dos doentes internados tinham idade inferior a 50 anos e 23% menos de 65 anos.[4]

Ao longo dos 10 anos avaliados constatou-se que o peso dos internamentos por PAC apresentou uma tendência crescente, documentada na evolução deste valor entre os períodos de 2000-2004 a 2005-2009. Verificou-se um aumento da média da percentagem dos internamentos de 3,3% para 4,2%, o que corresponde a um incremento de 27,3% de 2000-2004 para 2005-2009.[4] Em termos populacionais, o número de internamentos correspondeu a 3,61 internamentos por 1 000 habitantes/ ano[4] um valor igualmente superior ao documentado em Portugal continental, no período de 1998 a 2000, de 2,66 internamentos por 1 000 habitantes.[5]

Nos países mais desenvolvidos, a PAC representa a primeira causa de morte por doença infecciosa[6] e, de acordo com os últimos dados disponíveis nos Estados Unidos da América (EUA), foi a nona causa de morte em 2010.[7] Neste país, num estudo realizado em 1996 e envolvendo mais de 33 000 doentes, a mortalidade associada à PAC foi avaliada em 13,6% nos doentes com internamento hospitalar, aumentando para 36,5% nos doentes admitidos em Unidades de Cuidados Intensivos (UCI).[8] Num estudo posterior realizado nos EUA de 1987 a 2005 e envolvendo mais de dois milhões de doentes com idade ≥ 65 anos, a mortalidade aos 30 dias ajustada para a idade e género diminuiu de 13,5 para 9,7%.[9]

Nos países europeus, a mortalidade atribuível à PAC apresenta grandes variações. Numa revisão publicada em 2011 por Welte et al[1] com mais de três dezenas de estudos realizados em nove países europeus, verificou-se uma relação significativa entre o risco de mortalidade intra-hospitalar e o aumento de idade, com taxas de letalidade intra-hospitalar que variaram entre os 1,0 e os 43,0%, de acordo com as características das populações avaliadas, nomeadamente a idade (e.g., ≥ 65 anos), presença de comorbilidades, gravidade (e.g., envolvimento multilobar, choque séptico, necessidade de admissão em UCI), estado imunológico, resposta terapêutica e sensibilidade aos antimicrobianos.

Em Portugal, no triénio de 1998 a 2000, a taxa de letalidade intra-hospitalar dos adultos internados com o diagnóstico principal de PAC foi de 17,3%.[5] À semelhança dos internamentos hospitalares, a letalidade intra-hospitalar aumentou para 20,4% no período de 2000 a 2009.[10] Contudo, dada a crescente hospitalização da morte é de considerar a possibilidade deste valor poder estar sobrevalorizado pela inclusão de episódios de pneumonia de fim de vida.

A letalidade variou de acordo com a idade, com valores de 5,0% nos adultos com idade < 50 anos e de 22,1% e 24,1% nos indivíduos com idades ≥ 50 e ≥ 65 anos, respetivamente.[10] A PAC foi responsável por óbitos em todos os

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grupos etários mesmo em indivíduos jovens previamente saudáveis, verificando-se o valor mais baixo de letalidade de 2,7% no grupo etário dos 25 aos 29 anos.[10] Em 3,4% dos internamentos ocorreu ventilação mecânica invasiva com uma mortalidade média nestes doentes de 44,3%.[10]

Em conclusão, em Portugal continental verificou-se um aumento significativo dos internamentos hospitalares por PAC, que se traduz num acréscimo do impacto desta doença ao nível da saúde da população e na utilização de recursos do país. Em média, no período de 2000 a 2009, foram internados diariamente 81 adultos com pneumonia da comunidade dos quais 16 faleceram no decurso desse internamento.

CONFLITO DE INTERESSES

O autor declara não ter nenhum conflito de interesses relativamente ao presente artigo.

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5.3. Intra-hospital mortality for Community-Acquired Pneumonia in mainland Portugal between 2000 and 2009
(Artigo N.º 3)

Autores: Francisca Teixeira Lopes, Ana Cysneiros, Ana Dias, Vera Durão, Fernanda Paula, Margarida Serrado, Baltazar Nunes, António Diniz, Filipe Froes

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ORIGINAL ARTICLE

Intra-hospital mortality for community-acquired pneumonia in mainland Portugal between 2000 and 2009

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ORIGINAL ARTICLE

Intra-hospital mortality for community-acquired pneumonia in mainland Portugal between 2000 and 2009

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KEYWORDS
Community-acquired pneumonia;
Mortality;
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Inpatient mortality

Abstract
Introduction: Community-acquired pneumonia (CAP) remains a common and serious infection with wide variability in intra-hospital mortality.
Methods: We performed a retrospective analysis of adult patients admitted with CAP in mainland Portugal between the years 2000 and 2009.
Results: The intra-hospital mortality rate was 20.4% with deaths in all age groups. The average age of deceased patients was 79.8 years, significantly higher than surviving patients with 71.3 years. Patients aged 50 or more presented a relative risk of death 4.4 times the risk of patients under this age group. Likewise, in patients aged 65 or more the risk of death was 3.2 times the risk of patients <65 years. Men died more at a younger age than women, the men who died were, on average, 4 years younger than women, 78.1 vs 82.1 years old. Relative risk of death in men was 17% higher than women after adjustment for year of admission and age.
Conclusion: CAP remains an important cause of hospital mortality in all age groups.
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Introduction

Community-acquired pneumonia (CAP) is an important cause of morbidity and mortality as well as expenditure of health resources. A higher incidence of this disease was reported in men and older patients.[1]

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Several studies[2–4] in the last decade showed an increase in hospital admissions for CAP. Portugal was no exception.[5] Between 2000 and 2009 CAP was responsible for 3.7% of all hospital admissions which increased to 7% in patients ≥65 years of age.[5]

CAP is the leading cause of death by infectious disease in developed countries,[6] it is the eighth cause of death in the United States (US) in 2014.[7] In a US study with 33,000 patients conducted in 1996, CAP intra-hospital mortality was 13.6% increasing to 36.5% in ICU patients.[8]

In European countries, mortality due to CAP varies. In a 2012 review with more than 30 studies performed over 9 European countries, Welte et al.[1] concluded that variability of intra-hospital mortality in CAP was significantly related to several factors. This led to mortality rates of between 1.0% and 43% depending on age (≥65 years), co-morbidities, severity (multilobar pneumonia, septic shock, ICU admission), immune status, antibiotic sensitivity and response to treatment.

In Portugal, the mortality rate in adults admitted with CAP between 1998 and 2000 was 17.3% without gender predominance.[9] Mortality was greater in older patients, ranging from 4.5% in those younger than 50 years, 19.4% in patients ≥50 years and 21.4% in those older than ≥65 years.[9]

The present study aims to describe the evolution of intra-hospital mortality within the Portuguese adult population admitted with CAP between 2000 and 2009 and understand its distribution by age and gender.

Methods

Data was gathered through the Central Administration of the National Health System (NHS) which has clinical data for all patients admitted to Portuguese NHS hospitals. This covers nearly the entire resident population of mainland Portugal. Medical data, including diagnosis and procedures, were encoded from the discharge summaries by trained physicians using the *International Classification of Diseases, 9th Revision – Clinical Modification* (ICD-9-CM).

In this study, we retrospectively analyzed the hospital admissions of adults with a primary diagnosis of pneumonia (ICD-9-CM 480-486 and 487.0) between the years 2000 and 2009. We then analyzed all inpatient deaths regardless of the length of hospital stay. These codes excluded tuberculosis pneumonia, obstructive pneumonia (e.g. associated with lung cancer), patients under 18 years of age and those for whom pneumonia was not the main diagnosis. As ICD-9-CM does not specify whether pneumonia is community acquired, we excluded patients with HIV (ICD-9-CM 042-044 and/or diagnosis-related groups 488, 489 and 490), individuals who were immunocompromised by anti-cancer or immunosuppressive treatment (external cause of disease code E933.1) and transplant recipients (V42).

Patient anonymity was maintained throughout clinical analysis. Comparison of the mean age between groups was performed using the Student's *T* test or the Mann–Whitney test when the assumptions of the *T* test were not observed. The risk of death was compared between age groups, gender and year of admission with the chi-squared test. The relative risk of inpatient death was calculated for each group as well as the 95% confidence interval. To measure the effect of each variable (age group, gender and year of admission) on the risk of death adjusted to the other variables, a log-binomial regression was used. All tests used had a significance level set at 5%. Data analysis was performed using SPSS20 and STATA SE 11.

Table 1 Evolution of intra-hospital mortality rate between 2000 and 2009.

Year	Total admissions	Deaths (%)	
2000	23,679	4046	(17.1%)
2001	22,442	4147	(18.5%)
2002	26,093	4930	(18.9%)
2003	27,978	5549	(19.8%)
2004	26,582	5366	(20.2%)
2005	31,302	6569	(21.0%)
2006	29,131	6320	(21.7%)
2007	33,726	7235	(21.5%)
2008	34,083	7652	(22.5%)
2009	39,011	8111	(20.8%)
2000–2004	126,774	24,038	(19.0%)
2005–2009	167,253	35,887	(21.5%)
Total (2000–2009)	294,027	59,925	(20.4%)

Results

Annual intra-hospital mortality rates

Between the years 2000 and 2009, 294,027 adults were admitted to hospital with a main diagnosis of CAP. Of those, 59,925 (20.4%) died during their hospital admission.

Table 1 represents the inpatient mortality rate per year of admission between 2000–2004 and 2005–2009. The annual mortality rate showed a steady increase between the period 2000–2004 and 2005–2009 with a constant rise of 13.2%, except for the years 2007 and 2009.

Age and gender characterization

The patients admitted with a primary diagnosis of CAP had a mean age of 73.1 years (standard deviation – SD: 16.0). The deceased patients had a mean age of 79.8 years (SD: 11.3) and a median age of 82 years. This was significantly higher than the mean age of the surviving patients with 71.3 years ($p < 0.01$).

The inpatient mortality rate for male patients was 20.7% while in female population it was 20.0% ($p < 0.01$). Within the total of deceased patients, 56.5% were male with a mean age of 78.1 years and 43.5% were female with a mean age of 82.1 years. The difference between the mean ages in both groups was statistically significant ($p < 0.01$).

There were deaths in all age groups, however, the lowest mortality rate was observed in those aged 29 years with a mortality rate of 1.7%.

Table 2 represents the mortality rate of admitted patients by gender and age group (<50, ≥50, <65, ≥65, <75, ≥75 years).

Regardless of gender, the risk of death increased with age. The relative risk of death for patients aged 50 or more

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Table 2 Intra-hospital mortality by gender and age groups (age inferior or equal to and greater than 50, 65 and 75 years).

	Male			Female			Total		
Age groups (years)	Admitted patients	Deaths (%)		Admitted patients	Deaths (%)		Admitted patients	Deaths (%)	
<50	19,167	1059	(5.5%)	11,137	456	(4.1%)	30,304	1515	(5.0%)
≥50	144,311	32,770	(22.7%)	119,411	25,640	(21.5%)	263,723	58,410	(22.1%)
<65	41,855	3527	(8.4%)	23,520	1388	(5.9%)	65,376	4915	(7.5%)
≥65	121,623	30,302	(24.9%)	107,028	24,708	(23.1%)	228,651	55,010	(24.1%)
<75	77,186	9686	(12.5%)	45,528	4259	(9.4%)	122,715	13,945	(11.4%)
≥75	86,292	24,143	(28.0%)	85,020	21,837	(25.7%)	171,312	45,980	(26.8%)
Total	163,478	33,829	(20.7%)	130,548	26,096	(20.0%)	294,027	59,925	(20.4%)

was 4.4 times (CI95% 4.2–4.7) the risk for those under this age group. In the population ≥65 years the relative risk of death was 3.2 times (CI95% 3.1–3.3) the risk of the <65 years population ($p < 0.01$).

Table 3 represents the annual evolution of mean age and mortality rate in patients admitted and deceased between the years 2000 and 2009. Except for 2009, there was a consistent annual increase in the mean age as well as mortality rate.

Adjusted mortality rate in admitted patients (year, age and gender)

Table 4 represents the relative risk of death adjusted for year of admission, age and gender. The relative risk of death varied significantly between 2001 and 2009 when compared to 2000.

Data shows a steady increase in mortality rate by age group, with a small variation of relative risk after adjusting for year of admission and gender.

The risk of death was higher in males and this difference was even higher when adjusted for year of admission and age. Men had a 17% higher relative risk of death than women.

Discussion

From 2000 to 2009 the overall intra-hospital mortality rate for patients admitted with CAP in mainland Portugal was 20.4%. This is within the range observed in a European review published in 2012[1] with an intra-hospital mortality rate ranging between 1% and 43%. Like the European study in our analysis mortality also increased with age, with those ≥75 having a mortality rate of 26.8%, more than twice than those <75, which had 11.4% mortality rate. This was irrespective of year of admission and gender. There were deaths in all age groups with a highlight 5.0% mortality rate in patients younger than 50 years old. Over the studied period inpatient mortality rate showed a steady increase, with two exceptions: 2007 and 2009. These accompanied changes in the mean age of hospitalized and deceased patients. The average age of deceased patients was significantly higher, 79.8 years, against 71.3 years in surviving patients.

After adjustment for age and gender, the increase in the relative risk of death during hospitalization over the years maintained statistical significance, with an 11% raise between 2000 and 2009. Patients aged 50 or more had a relative risk of death 4.4 times the risk of patients under this age group. Likewise, in patients aged 65 or more the risk of death was 3.2 the risk of patients <65. More men

Table 3 Mean ages and intra-hospital mortality rates of admitted and deceased patients between 2000 and 2009.

Year	Mean age (years)		Intra-hospital mortality rate (%)
	Admitted patients (*N*: 294,027)	Deceased patients (*N*: 59,925)	
2000	70.1	78.1	17.1
2001	71.3	78.3	18.5
2002	71.6	79.0	18.9
2003	72.1	79.3	19.8
2004	73.3	79.7	20.2
2005	73.8	80.0	21.0
2006	73.8	80.0	21.7
2007	74.2	80.5	21.5
2008	75.0	80.8	22.5
2009	73.6	80.7	20.8
2000–2009	73.1	79.8	20.4

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Table 4 Intra-hospital mortality adjusted for year of admission, age groups and gender.

	Intra-hospital mortality	Crude relative risk	95% confidence interval	Adjusted relative risk	95% confidence interval
Year					
2000	17.09	Reference		Reference	
2001	18.48	1.08	1.04–1.12	1.04	1.00–1.08
2002	18.89	1.11	1.07–1.15	1.07	1.03–1.11
2003	19.83	1.16	1.12–1.20	1.10	1.06–1.14
2004	20.19	1.18	1.14–1.23	1.09	1.05–1.13
2005	20.99	1.23	1.19–1.27	1.12	1.08–1.16
2006	21.70	1.27	1.26–1.32	1.14	1.10–1.18
2007	21.45	1.26	1.21–1.30	1.13	1.09–1.16
2008	22.45	1.31	1.27–1.36	1.15	1.11–1.19
2009	20.79	1.22	1.18–1.26	1.11	1.07–1.14
p-value	<0.001				
Age groups					
18–29	3.47	Reference		Reference	
30–49	5.43	1.56	1.36–1.79	1.54	1.34–1.76
50–64	9.69	2.79	2.45–3.18	2.74	2.41–3.12
65–74	15.75	4.54	3.99–5.16	4.47	3.94–5.08
75–84	23.31	6.71	5.91–7.62	6.65	5.85–7.55
≥85	32.03	9.23	8.12–10.48	9.28	8.17–10.54
p-value	<0.001				
Gender					
Male	20.69	1.04	1.02–1.05	1.17	1.15–1.18
Female	19.99	Reference		Reference	
p-value	<0.001				

died and at a younger age than women. The mean age of deceased men was 78.1 years, 4 years younger than the mean age of deceased women which was 82.1 years. Relative risk of death in men was 17% higher than in women after adjustment for year of admission and age.

Our study has several limitations. Primarily, it is a retrospective study that uses an administrative database with coded information from discharge summaries. However, in Portugal, codification is done only by medical doctors with specific training. The process is regularly internally and externally audited which contributes to guarantee accuracy. Due to the lack of a specific CAP code in ICD-9-CM, we only analyzed adult hospital admissions where the main diagnosis was pneumonia. Patients with a main diagnosis of respiratory failure or sepsis associated to a secondary diagnosis of pneumonia were not included. The latter could be associated with a higher mortality rate[10] but also with nosocomial pneumonia. Still, we acknowledge the possibility that some cases of hospital-acquired pneumonia could have been included in our study. This is possible due to coding error but also because the database does not allow for discrimination of pneumonia after recent hospital discharge, hence pneumonia that is not strictly community acquired. Similarly, it is not possible to identify patients living in nursing homes or using long-term care facilities, hence it is expected that cases of healthcare-associated pneumonia have been included, particularly in the elderly. However, this concept and its inclusion in nosocomial pneumonia remain the source of controversy for some authors in Europe.[11] The methodology used made it impossible to exclude all rehospitalizations of the same patient with pneumonia during the period studied, so the calculated values refer to hospital admissions.

The greater accessibility to hospital institutions and the fear of dying at home, both for patients and their families, might explain the inclusion of patients with end-of-life pneumonia. These will likely have a higher impact in the older age groups.

The methodology used allowed for the exclusion of patients with tuberculosis, obstructive pneumonia, those with HIV, recipients of transplanted organs, the immunosuppressed and those under treatment for cancer.

In this study, the length of hospitalization was not assessed, which could have contributed to a greater specificity of the methodology.[12] It was neither possible to obtain information on mortality at 30 days after hospital admission or to identify the subset of patients requiring ICU admission. Our database had no information on pneumonia severity, co-morbidities or immunization status, regarding influenza or pneumococcal disease. Despite these limitations, the methodology used has been considered valid and is applied in multiple studies carried out in different countries.[3,5,9,13–15]

This study has the advantage of analysing a period of 10 years, minimizing the impact of years that deviate from normality, such as 2009, when the A(H1N1) influenza pandemic occurred. Regarding the year 2009, there were more CAP admissions[5] and this could be related to the

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influenza pandemic, but, this did not impact on intra-hospital mortality, which was lower in 2009 than in previous years. Mean age of admission could be a contributing factor to lower mortality since it was lower in 2009. According to Portuguese official data there were 124 deaths attributable to the influenza pandemic through serologic testing (1.17 deaths per 100,000 inhabitants) with a mean age of 47.6 years.[16] In summary, during the influenza pandemic there were more admissions of young patients with CAP.

The database analysis could not identify factors contributing to the annual increase in intra-hospital mortality rates even after adjusting for age, gender or the higher risk of death in males. Factors such as smoking, alcoholism, severity of pneumonia, clinical management of the disease and, above all, the increasing prevalence of comorbidities in the Portuguese population may be associated with the increase in mortality.

CAP remains an important cause of hospital mortality in all age groups. Further studies are needed to better understand which factors are associated with the annual increase in intra-hospital mortality rates. However our study fully justifies the adoption of lifestyle-modifying measures as well as greater appreciation of anti-influenza and anti-pneumococcal vaccinations.[17]

Conflicts of interest

Dr. Froes reports personal fees and non-financial support from Pfizer, personal fees and non-financial support from MSD, personal fees and non-financial support from TEVA, non-financial support from Sanofi, non-financial support from AstraZeneca, non-financial support from Bayer, personal fees from Novartis, outside the submitted work.

Dr. Teixeira-Lopes and the other co-authors have nothing to disclose.

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5.4. Direct Costs Related to the Admissions of Adults with Community Acquired Pneumonia in Mainland Portugal during the 2000-2009 Period (Artigo N.º 4)

Autores: Filipe Froes, António Diniz, Patrícia Barbosa, Vera Durão, Francisca Teixeira Lopes, Ana Cysneiros, Ana Dias, Margarida Serrado, Cristina Bárbara, Ana Escoval

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Direct Costs Related To The Admissions Of Adults With Community Acquired Pneumonia In Mainland Portugal During The 2000-2009 Period

F. Froes[1], A. Diniz[2], P. Barbosa[3], V. Durao[2], F. Teixeira Lopes[2], A. Cysneiros[2], A. Dias[2], M. Serrado[2], C. Barbara[2], A. Escoval[3]

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Introduction: Admissions of adults with Community Acquired Pneumonia (CAP) in Continental Portugal during the 2000-2009 period accounted for 3,7% of all the admissions registered in this period, with 81 admissions per day, one admission at every 18 minutes, and 16 deaths per day, one death at every 90 minutes. Although with a clinical impact, there is no data on the direct costs of these admissions.
Methods: A retrospective analysis of the data base of the Portuguese Central Administration of the Health System, which contains clinical and administrative information of all the hospital admissions in the National Health Service, was performed. All admissions of adults with a primary discharge diagnosis of pneumonia (encoded as 480–486 and 487 by the International Classification of Diseases, 9th Revision Clinical Modification - ICD-9-CM) between 2000 and 2009 were included. Patients aged under 18 years old were excluded as well as patients in whom pneumonia was not the primary diagnosis and those immunosuppressed, either due to infection by the human immunodeficiency virus (ICD-9-CM: 042-044), immunosuppressive therapies such as antineoplastic (E933.1 code – external cause disease) or post-transplantation (V42). Patients' anonymity was assured during the entire process.
Results: Between 2000 and 2009, 294.026 hospital admissions were analyzed with an overall direct cost of approximately 800 M€. The mean direct cost per admission was 2.706€ which corresponds to a mean daily expense of 218.050€ with a growing trend over the years.
Conclusion: The direct costs related to the admissions of adults with CAP in Continental Portugal during the 2000-2009 period had a high economic impact, accounting for 1 million euros every 4 days and 14 hours.

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Direct costs related to the admissions of adults with Community Acquired Pneumonia in Mainland Portugal during the 2000-2009 period

Filipe Froes[1], António Diniz[1], Patrícia Barbosa[2], Ana Cysneiros, Vera Durão[1], Francisca Teixeira Lopes[1], Ana Dias[1], Margarida Serrado[1], Cristina Bárbara[1] e Ana Escoval[2]

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Introduction: Admissions of adults with Community Acquired Pneumonia (CAP) in Mainland Portugal (10 million inhabitants) during the 2000-2009 period accounted for 3,7% of all the admissions registered in this period, with 81 admissions per day, one admission at every 18 minutes, and 16 deaths per day, one death at every 90 minutes. Although with a clinical impact, there is no data on the direct costs of these admissions

Methods: A retrospective analysis of the data base of the Portuguese Central Administration of the Health System, which contains clinical and administrative information of all the hospital admissions in the National Health Service, was performed. All admissions of adults with a primary discharge diagnosis of pneumonia (encoded as 480–486 and 487 by the International Classification of Diseases, 9th Revision Clinical Modification - ICD-9-CM) between 2000 and 2009 were included. Patients aged under 18 years old were excluded as well as patients in whom pneumonia was not the primary diagnosis and those immunosuppressed, either due to infection by the human immunodeficiency virus (ICD-9-CM: 042-044), immunosuppressive therapies such as antineoplastic (E933.1 code – external cause disease) or post-transplantation (V42). Patients' anonymity was assured during the entire process.

Mainland Portugal
Adults (2000 a 2009)
294,026 admissions

Direct cost of hospital admission: **2.706€**
Admission with live outcome: **2.515€**
Admission with deceased outcome: **3.457€**
+37,5%

Total: 795,884,142€ ➔ 80 M€ / year
Daily cost: 218,050€ / day
1 M€ every 4,6 days

Results: Between 2000 and 2009, 294,026 hospital admissions were analyzed with an overall direct cost of approximately 800 M€. The mean direct cost per admission was 2.706€ which corresponds to a mean daily expense of 218,050€ with a growing trend over the years.
The mean cost among surviving patients was 2,515€. The mean cost of hospital admission for patients that died was 3,457€, an increase of 37.5% compared to surviving patients.

Conclusion: The direct costs related to the admissions of adults with CAP in Continental Portugal during the 2000-2009 period had a high economic impact, accounting for 1 million euros every 4 days and 14 hours.

5.5. PSI, CURB-65, SMART-COP or SCAP? And the winner is... SMART DOCTORS (Artigo N.º 5)

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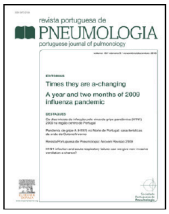

EDITORIAL

PSI, CURB-65, SMART-COP or SCAP? And the winner is... SMART DOCTORS

PSI, CURB-65, SMART-COP ou SCAP? E o vencedor é... SMART DOCTORS

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EDITORIAL

PSI, CURB-65, SMART-COP or SCAP? And the winner is... SMART DOCTORS

PSI, CURB-65, SMART-COP ou SCAP? E o vencedor é... SMART DOCTORS

Community-acquired pneumonia (CAP) is one of the most common diseases in adults with an estimated average annual incidence of 5 to 11 cases per 1000 inhabitants,[1] which increases significantly with age.[2] It is a major cause of hospital admission but the percentage of patients hospitalized for CAP varies greatly depending on country or region, the populations studied and the way the health systems are organised. In Portugal, it is estimated that 25 to 50% of adults with CAP are admitted to hospital[3] and, in the period from 2000 to 2009, CAP was one of the principle causes of hospitalization, representing 3,7% of total adult hospital admissions.[4]

Although the majority of patients are treated as outpatients, hospital admissions for treatment of patients with CAP represent a big percentage of the cost of treating CAP patients. Studies carried out in the United States of America (USA), at the end of the last century, worked out that the total annual cost was 8,4 billion US dollars, of which 8,0 billion (95%) was the result of hospital admission.[5] To deal with this, Michael Fine *et al* developed the first score for CAP, the *Pneumonia Severity Index* (PSI), with the goal of predicting mortality and identifying patients at low risk of mortality who did not need to be admitted to hospital.[6] The PSI stratifies patients into 5 risk classes, based on evaluation of more than twenty clinical and laboratory parameters, heavily weighted for age and comorbidities.[7] The complexity of the PSI, led to the development of another score, the CURB-65 (acronym for Confusion, Urea, Respiratory rate, Blood pressure and age $\geq$65) by the British Thoracic Society.[8]

Various studies have evaluated the PSI and the CURB-65 in the same populations with comparable results for predicting mortality and identifying low-risk patients, although in one study the CURB-65 had better results in predicting mortality in the most serious cases.[7]

It should be pointed out that neither the PSI nor the CURB-65 were developed to identify patients needing to be referred to the Intensive Care Units (ICU), although the CURB-65 does appear to be more precise than the PSI in predicting admission to ICU.[9]

In 2001, the American Thoracic Society (ATS) made the following recommendations for CAP in order to identify patients with serious pneumonia and predicted admission into ICU using major and minor criteria.[10] Severe CAP was defined by the presence of one of two major criteria (dependence on mechanical ventilation or septic shock) or 2 of three minor criteria (systolic blood pressure $\leq$90 mm Hg, multilobar involvement or PaO_2/FIO_2 $\leq$250).[10] In 2007, joint recommendations by the Infectious Diseases Society of America (IDSA) and the ATS[11] increased the minor criteria to nine, patients needing to meet at least 3 minor criteria to be defined as severe CAP; however, there were no gains in terms of sensitivity or specificity over the 2001 criteria.[12]

More recently, two new scores have emerged: the SMART-COP (acronym for Systolic blood pressure, Multilobar infiltrates, Albumin, Respiratory rate, Tachycardia, Confusion, Oxygen and pH) developed in Australia,[13] and SCAP (Severe CAP) developed in Spain,[14] which utilizes major criteria (pH and systolic blood pressure) and minor ones (confusion, urea, respiratory rate, multilobar infiltrates, oxygen and age $\geq$80). Although many of the parameters evaluated are common to all scores, these two new scores differ from the PSI and CURB-65 in that they do not present the same level of validation and their principle goal is identification of patients with severe pneumonia who need to be referred to ICU. In the actual PJP edition C. Ribeiro et al. compare these new scores with the two previous ones.[15]

All the existing scores have advantages and limitations. The main advantages are the prediction of risk of mortality and serious progressive complications, cutting down costs by reducing expensive hospital human resources on low-risk patients and in the early recognition of the most seriously ill patients so that they benefit from rapid referral to the ICU.[7]

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Another important advantage is the use of scores in clinical research.[7] In terms of limitations, the different scores vary in terms of levels of validation and accuracy, particularly among certain age groups, such as the oldest and the youngest. They do not properly take into account social factors and the degree of dependency which could affect the decision as to whether to admit to hospital and there is also the omission of important comorbidities like DPOC, immunosuppression and functional status. Very recently the Influenza A(H1N1) pandemic in 2009, provided the opportunity to check the lowest predictive value and usefulness of the different scores in patients with viral pneumonia.[16]

None of the current scores include acute phase inflammatory markers or biomarkers but preliminary data indicate that these, in particular procalcitonin, could improve the score risk stratification and thus increase their usefulness.[7]

In conclusion, these scores are useful tools but they cannot nor should they substitute medical evaluation and clinical reasoning. Ideally, the best strategic approach to CAP will always depend on experienced doctors (SMART-DOCTORS) who can apply their knowledge to the complexity and specific characteristics of the individual patients and can use the scores as supplementary information to make appropriate decisions for the population in question.

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5.6. Achoo, achis, ATCHIN! Vaccine you…
(Artigo N.º 6)

Autores: Filipe Froes, Francesco Blasi, Antoni Torres

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EDITORIAL
RESPIRATORY INFECTION

Achoo, achis, ATCHIN! Vaccine you...

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EDITORIAL
RESPIRATORY INFECTION

Achoo, achis, ATCHIN! Vaccine you...

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Take every opportunity to act on modifiable risk factors for CAP. ATCHIN! http://ow.ly/lscV30i00iU

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Community-acquired pneumonia (CAP) is an important cause of morbidity, mortality and expenditure of health resources. Globally, lower respiratory tract infection, which includes CAP, was the fourth leading cause of death in 2015 [1]. In developed countries CAP is the leading cause of death by infectious disease [2], and in 2014 it was the eighth cause of death in the USA [3].

Within the 28 countries that form the European Community, pneumonia and other acute lower respiratory tract infections are associated with an estimated annual expenditure of €46 billion in direct costs and disability-adjusted life-years (DALY) [4]. Together with the financial burden it is also important to acknowledge that CAP contributes to a high antibiotic usage which has future implications in the development of antibiotic resistance.

CAP can affect any age group, hence we are all at risk, even though some are more at risk than others. Several risk factors for CAP are well recognised and studied [5], including age above 65 years [6], alcoholism [7], cigarette smoking [8], immunosuppression [7], and comorbidities such as COPD [9], cardiovascular disease, cerebrovascular disease, chronic liver or renal disease, diabetes mellitus and dementia [10].

The increase in life expectancy and the growing prevalence of comorbidities [11] highlight the importance of pneumonia prevention but also the importance of adequate control of chronic conditions. For instance, the severity of airway obstruction in COPD has been linked with the incidence of CAP [12]. Likewise, immunosuppressive therapy, including the use of oral steroids, are important risk factors for the development of CAP [5, 13]. The increased risk of pneumonia is an important safety concern when prescribing immunosuppressive therapy [13].

A comprehensive analysis of studies in the adult population of western Europe from 2013 by Torres *et al.* [5] investigated the association between the incidence of CAP and age, comorbidities and lifestyle factors. The association and the weight of different modifiable risk factors lead to a bundle of lifestyle interventions

Note to the title: Achoo (English), achis (Spanish), atchim (Portuguese), atchis (Catalan), etciu (Italian), atchoum (French), hatschi (German), hatsjie (Dutch).

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TABLE 1 The ATCHIN acronym for modifiable risk factors for community-acquired pneumonia

	Risk factor	Recommendation
A	**A**lcohol	Reduce alcohol consumption
T	**T**obacco	Tobacco/smoking cessation
C	**C**hronic conditions and **C**omorbidities	Adequate management of chronic conditions and comorbidities
H	Dental **H**ygiene	Ensure good oral hygiene and regular dental appointments
I	**I**mmussupressive therapy and contact with **I**nfants and children	Judicious use of immunosuppressive drugs (including oral steroids) and avoidance of infants and children with lower respiratory tract infections
N	**N**utritional status	Dietary advice to ensure good nutritional status

Adapted from [5].

to reduce the risk of CAP in adults. These included smoking cessation, responsible alcohol consumption, dental hygiene, dietary advice to ensure good nutritional status, the avoidance of infants and children with lower respiratory tract infections, and vaccination against influenza virus and *Streptococcus pneumoniae*. Based on this bundle we propose an easy to remember acronym – ATCHIN – with a group of interventions to reduce the risk of CAP in adults that aims to simplify its implementation by healthcare professionals (table 1).

Achoos, Achis, ATCHIN! Bless you. In this case, vaccinate yourself and vaccinate your patients against influenza virus and *S. pneumoniae*. And take every opportunity to act on modifiable risk factors for CAP. ATCHIN!

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5.7. Consensus document for the prevention of respiratory infections in adults (Artigo N.º 7)

Autores: Filipe Froes, António Diniz, Carlos Robalo Cordeiro, Margarida Serrado, António Ramalho de Almeida

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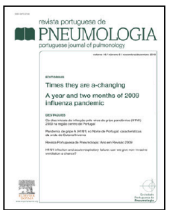

CONSENSUS

Consensus document for the prevention of respiratory infections in adults

Rev Port Pneumol. 2014;20(2):111–114

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CONSENSUS

Consensus document for the prevention of respiratory infections in adults

KEYWORDS
Prevention;
Respiratory infections;
Pneumonia;
Flu vaccination;
Pneumococcal vaccination

Abstract Infectious diseases are one of the principle causes of morbidity, mortality and drain on health resources worldwide. In recent years there has been an increase in the impact of respiratory infections, particularly in the Portuguese population. It is for this reason that the Portuguese Respiratory Society has presented a series of recommendations for the prevention of respiratory infections in adults. These recommendations include both general measures and vaccinations for flu and pneumococcal pneumonia.
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PALAVRAS-CHAVE
Prevenção;
Infeções respiratórias;
Pneumonia;
Vacina da gripe;
Vacina pneumocócica

Documento de Consenso para a prevenção das infeções respiratórias no adulto

Resumo As infeções respiratórias são uma das principais causas de morbilidade, mortalidade e consumo de recursos de saúde a nível global. Nos últimos anos tem-se assistido a um crescente impacto das infeções respiratórias, nomeadamente na população portuguesa. Assim, a Sociedade Portuguesa de Pneumologia apresenta um conjunto de recomendações para a prevenção das infeções respiratórias no adulto. Estas recomendações englobam medidas gerais e de vacinação antigripal e antipneumocócica.
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Respiratory infections are among the principal causes of morbidity, mortality and of demands on health resources at a global level.[1] Apart from the direct and indirect costs, what is of major concern is the associated high consumption of antimicrobial drugs and the consequent increased growth in resistance to this class of medicines, which could affect the use of some types of antibiotics in the near future.

In continental Portugal, recently published data relating to the period of 2000–2009 document the significant impact of respiratory infections and, in particular, of pneumonias. In this period hospital admissions for Community Acquired Pneumonia (CAP) represent 3.7% of the total number of adult hospital admission for all causes in National Health Service institutions.[2] In the age groups ≥50 and ≥65, hospitalization for CAP represents 5.5% and 7.0% of total admissions respectively.[2]

Given this national situation, there is a general consensus about the necessity for a rapid implementation of measures to prevent respiratory infections in adults.

These preventive measures against respiratory infection cover general measures and specific measures: vaccination against flu and antipneumococcal.

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Table 1 Recommendations for adult antipneumococcal vaccination.

Age	Groups at risk of invasive pneumococcal disease	VPC13	VPP23	
		Vaccination	Vaccination	Revaccination (after 5 years)
≥18	*Immunocompromised*: Congenital or acquired immunodeficiency HIV/AIDS Chronic renal failure Nephrotic syndrome Neoplastic diseases (e.g., haematological malignancies, lymphomas, multiple myeloma) Iatrogenic immunosuppression (e,g., long-term systemic corticotherapy, chemotherapy and radiotherapy) Solid organ transplant	Recommended	Recommended	Recommended
	Anatomical or functional asplenia (e.g., sickle cell anaemia and other hemoglobinopathies, congenital or acquired asplenia)	Recommended	Recommended	Recommended
	Cerebrospinal fluid leaks	Recommended	Recommended	Recommended
	Cochlear implants	Recommended	Recommended	Recommended
≥50	*Chronic co-morbidities*: Chronic respiratory diseases (includes chronic asthma under inhaled corticosteroid) Chronic cardiac diseases (excludes hypertension alone) Chronic liver diseases (e.g., cirrhosis) Diabetes mellitus (excludes patients controlled by diet only)	Recommended	Recommended	Recommended
≥65	*Individuals aged ≥65*	Recommended	Recommended	Not recommended

General measures

In the general measures, related to host defences, the following are recommended[3]:

- smoking cessation;
- control of chronic illnesses (diabetes mellitus, COPD, congestive heart failure, chronic renal failure, chronic liver disease, HIV/AIDS infection, etc.);
- judicious use of immunosuppressive therapies (including corticosteroids);
- alcohol counselling (including acute intoxication and chronic alcoholism);
- advice about dealing with cases of drug addiction;
- adequate nutritional status;
- gamma globulin IV immunotherapy in selected patients (IgG deficiency, multiple myeloma, chronic lymphocytic leukaemia, transplant patients).

Anti-flu vaccination

This endorses the Directorate-General of Health recommendation for vaccination against seasonal flu for the current season.[4] Health professionals and other professionals involved in front-line health care are a priority group for vaccination, because of the increased risk of contracting the illness and transmitting it to their families and their patients. Setting an example and the counselling about vaccination given by health professionals represent one of the principle success factors in keeping to vaccination targets.

Table 2 Recommendations for antipneumococcal vaccination in specific circumstances (adapted from[1,13]).

Condition	Vaccination recommendations (individuals not vaccinated)
HIV/AIDS	Early, preferably with lymphocytes TCD4$^+$ $\geq$ 200/mm^3; if TCD4$^+$ < 200/mm^3, vaccinate without waiting for immune reconstruction and consider revaccination after TCD4$^+$ $\geq$ 200/mm^3
Surgical splenectomy	In elective surgery, at least 2 weeks before surgery; in unplanned surgery, vaccinate 2 weeks after surgery
Autoimmune diseases	Early and before starting immunosuppressive therapy
Waiting for a solid organ transplant	Early, at least 2–4 weeks before transplant
Solid organ transplant	Start vaccination 6 months after transplant
Transplant of hematopoietic cells	Start vaccination 3–6 months after transplant
Neoplastic diseases in chemotherapy and/or radiotherapy	10–14 days before treatment or 3 months after finishing chemotherapy or radiotherapy. If the vaccine is administered during the course of chemotherapy consider whether to revaccinate 3 months after finishing treatment

Pneumococcal vaccination

In Portugal two pneumococcal vaccines are available for adults aged 18 and above, a pneumococcal polysaccharide vaccine 23-valente [(*Pneumo 23*®) VPP23] with 23 serotypes (1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 20, 22F, 23F, 33F) and a pneumococcal conjugate vaccine 13-valente [(*Prevenar 13*®) VPC13] with13 serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F). Both vaccines are intramuscular and VPP23 can also be administered subcutaneously.[5,6]

For adults, vaccines are indicated for the prevention of invasive pneumococcal diseases by the serotypes included in the vaccine. The bacteraemia secondary to pneumonia is the main manifestation of invasive pneumococcal disease in adults, representing about 75% of cases of invasive disease in the adult population[7] and more than 80% in those $\geq$65.[8]

At the present time, we are waiting for the results of studies about the efficacy of VPC13 in the prevention of pneumonia in adults.

Epidemiological surveillance programmes on invasive pneumococcal disease and its serotypes at a national level are crucial for the evaluation of the effectiveness of anti-pneumococcal vaccines and recommendations for their utilization. According to the latest data available at a national level, relating to the period 2006–2008, from a total of 1100 isolates of *Streptococcus pneumoniae* in adults with an invasive pneumococcal disease, 68% of the serotypes identified were included in VPC13 and 84% in VPP23.[9]

Table 1 presents recommendations for antipneumococcal vaccinations according to the risk of invasive pneumococcal disease.[7,8,10–13]

In adults who are indicated for antipneumococcal vaccination, the following dosing schedule is suggested[10]:

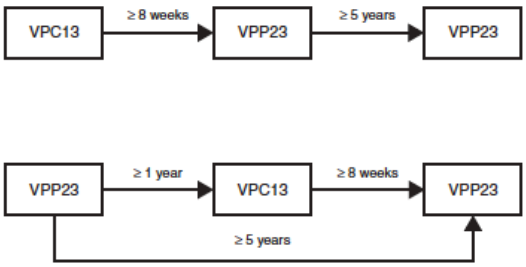

Figure 1 Schedule for antipneumococcal vaccination in non-vaccinated individuals or previously vaccinated with VPP23.

- adults who have not previously been vaccinated should first receive VPC13 followed by a dose of VPP23 at least 8 weeks later;
- adults who have already been vaccinated with VPP23 should only receive VPC13 at least one year after the last vaccination of VPP23;
- for adults with indication for revaccination with VPP23, the second dose must only be given at least 5 years after the first dose of VPP23 and at least 8 weeks after administration of VPC13.

Revaccination with VPC13 is not recommended and in the case of VPP23, revaccination should only be done once (Fig. 1).

Pneumococcal vaccines should be administered at the most propitious time for the immune system to respond; Table 2 presents an optimization calendar of vaccinations for certain clinical conditions (adapted[13]).

The influenza and pneumococcal vaccines can be given at the same time, preferably in different arms.

Conclusions

The recommendations presented in this document should be subject to clinical judgement in relation to the individual cases.

This document will be subject to periodic revisions in order to include the scientific evidence of future studies and knowledge about other measures and vaccines like, for example, the whooping cough which is available and recommended in some European countries.[14,15]

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5.8. Pneumococcal vaccination and chronic respiratory diseases (Artigo N.º 8)

Autores: Filipe Froes, Nicolas Roche, Francesco Blasi

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REVIEW

Pneumococcal vaccination and chronic respiratory diseases

This article was published in the following Dove Press journal:
International Journal of COPD

Filipe Froes[1]
Nicolas Roche[2]
Francesco Blasi[3,4]

Abstract: Patients with COPD and other chronic respiratory diseases are especially vulnerable to viral and bacterial pulmonary infections, which are major causes of exacerbations, hospitalization, disease progression, and mortality in COPD patients. Effective vaccines could reduce

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REVIEW

Pneumococcal vaccination and chronic respiratory diseases

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Abstract: Patients with COPD and other chronic respiratory diseases are especially vulnerable to viral and bacterial pulmonary infections, which are major causes of exacerbations, hospitalization, disease progression, and mortality in COPD patients. Effective vaccines could reduce the burden of respiratory infections and acute exacerbations in COPD patients, but what is the evidence for this? This article reviews and discusses the existing evidence for pneumococcal vaccination efficacy and its changing role in patients with chronic respiratory diseases, especially COPD. Specifically, the recent Community-Acquired Pneumonia Immunization Trial in Adults (CAPITA) showed the efficacy of pneumococcal conjugate vaccine in older adults, many of whom had additional risk factors for pneumococcal disease, including chronic lung diseases. Taken together, the evidence suggests that pneumococcal and influenza vaccinations can prevent community-acquired pneumonia and acute exacerbations in COPD patients, while pneumococcal vaccination early in the course of COPD could help maintain stable health status. Despite the need to prevent pulmonary infections in patients with chronic respiratory diseases and evidence for the efficacy of pneumococcal conjugate vaccine, pneumococcal vaccine coverage and awareness are low and need to be improved. Respiratory physicians need to communicate the benefits of vaccination more effectively to their patients who suffer from chronic respiratory diseases.

Keywords: COPD, COPD exacerbation, infection, pneumococcal vaccine

Introduction

Patients with chronic respiratory diseases (CRDs), especially those with COPD, exhibit altered lung defenses and frequently have multiple comorbidities, which include cardiovascular disease, diabetes, metabolic syndrome, chronic anemia, osteoporosis, depression, and cancer.[1–3] Such adverse conditions make these patients especially vulnerable to viral and bacterial pulmonary infections, which are major causes of exacerbations, hospitalization, and disease progression.[1,4,5] Pneumonic infections in COPD patients have a major impact on morbidity, mortality, and health-care costs.[6,7] Since vaccines are among the most effective means of preventing infectious diseases and their consequences, preventing pulmonary infections in COPD patients through vaccination could reduce the burden of COPD and its complications, as well as further declines in patient health. For many years, pneumococcal vaccination in adults has relied primarily on polysaccharide vaccines. More recently, however, a large study demonstrated the efficacy of pneumococcal conjugate vaccine (PCV) in older adults (Community-Acquired Pneumonia Immunization Trial in Adults [CAPITA]), in which many of the participants had additional risk factors for pneumococcal disease.[8] Following these new developments, a symposium was held at the 2016 European Respiratory Society International Congress (September 5, 2016, London, UK) to examine and discuss the changing role of pneumococcal vaccination in patients with CRD, especially COPD. One major aim of these discussions was to document whether vaccination

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with PCV should be included among other strategies known to benefit COPD patients, such as smoking cessation, respiratory therapy, trigger avoidance, and influenza vaccination, to reduce the risk of exacerbations and respiratory events.

Pneumococcal diseases in patients with chronic respiratory diseases

The global burdens of respiratory diseases remain among the highest of all diseases and the most frequent causes of death.[9,10] COPD and lower respiratory tract infections (LRTIs) are the third- and fourth-leading causes of death, respectively, after heart disease and stroke,[9,11] with ~55% of all LRTI deaths attributable to pneumococcal pneumonia.[10] In Europe, pneumonia is the leading cause of respiratory hospitalizations and the second leading cause of death due to respiratory disease after lung cancer.[12] The situation is compounded by the nearly 23 million Europeans with moderate–severe COPD who account for 1.1 million hospitalizations and 150,000 deaths each year.[12] COPD is frequently associated with comorbidities that contribute greatly to patient mortality. Among these, coronary artery disease and congestive heart failure play a major role.[2] Hospitalizations and deaths due to COPD can be expected to rise in the future as the disease progresses in the 17 million additional persons in the EU, who are estimated to be living with mild-stage COPD.[12] Currently, pneumonia, COPD, and asthma account for 55.7% of respiratory hospital admissions and 47.3% of respiratory deaths in the EU.[12]

Patients with COPD, other CRDs, or other underlying chronic conditions are at high risk of community-acquired pneumonia (CAP), which imposes a substantial disease burden on the European population. Each year, there are an estimated 3.37 million cases of CAP, almost a third of which require hospitalization.[12] A retrospective cohort analysis of health-care claims in the US determined the risk of pneumococcal pneumonia to be 2.7 times higher in adults ≥65 years old compared to adults 50–64 years old (Figure 1).[13] In general, the incidence of pneumococcal pneumonia increased after the age of 65 years and was severalfold higher in persons of all ages living with chronic diseases, such as diabetes, heart disease, asthma, or lung disease, or with underlying conditions, such as smoking or alcoholism, compared to those with no known risk conditions. Among adults ≥65 years old, the incidence of pneumococcal pneumonia was 7.7-fold higher in persons with CRD compared to those without comorbidity (Figure 1). Further, incidence increased exponentially in patients who had multiple comorbidities ("risk stacking"). In patients with three at-risk conditions, incidence was 9–16 times higher than in healthy adults without any known risk factors and twice as high as in immunocompromised patients, who are considered to be at high risk.[13]

The prevalence of chronic conditions that put people at risk is also high, as shown in another US study in which 32.1% of adults 45–64 years old and 61.6% of adults ≥65 years of age had at least two chronic conditions and were considered at high risk of CAP.[14] As the mean age of the population continues to increase, the prevalence of persons with multiple chronic conditions is also expected to rise.[14] In Europe, the incidence of CAP was found to be more than 20-fold higher in persons with COPD (22.4 per 1,000 person-years) than in the general population (1.07–1.2 per 1,000 person-years),

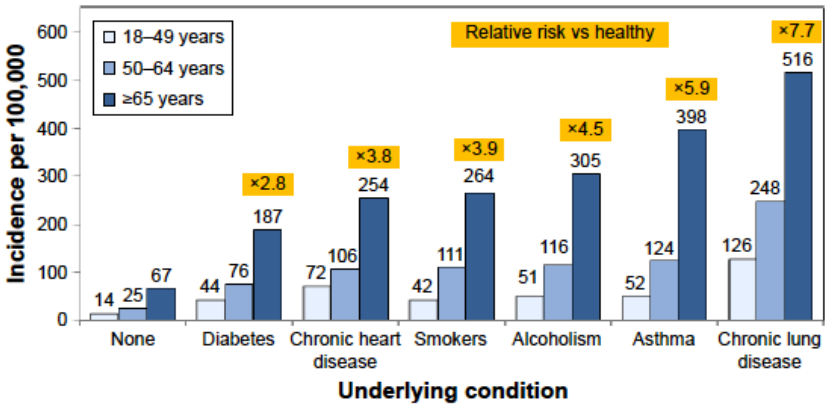


Figure 1 Incidence of pneumococcal pneumonia in adults with underlying conditions in the US, 2007–2010.
Notes: By age group and chronic condition. The retrospective cohort analysis utilized health-care claims data from 2007 through 2010 to compare the rates of pneumococcal disease among persons with certain chronic conditions versus their age-matched healthy counterparts. The databases included medical claims (ie, facility and professional services) and outpatient pharmacy claims from private US health plans. Data from Shea et al.[13]

with the incidence dramatically higher in persons with severe COPD (forced expiratory volume in 1 second [FEV_1] <50% of expected).[15,16] In Sweden, the risk of severe/invasive pneumococcal disease (IPD) was fivefold higher in persons with COPD or pulmonary fibrosis and twice as high in persons with asthma than in the general population.[17]

COPD patients may be more susceptible to respiratory infections, because their mucociliary clearance mechanisms are impaired, and production of the specific cell adhesion molecules that mediate attachment of bacteria and viruses is increased in their airways. Expression of platelet adhesion factor receptor (a cell adhesion molecule for *Streptococcus pneumoniae* and untypable *Haemophilus influenza*) and more recently ICAM1 (a cell adhesion molecule for rhinovirus) have been found to be significantly elevated in COPD patients and smokers compared to normal controls.[18,19] Elevated levels of these proteins may increase the risk of respiratory infection and bacterial colonization. In addition, certain treatments, such as inhaled corticosteroids, can further increase the risk of pneumonia in COPD patients. This risk appears to increase with the dose of the drug, regardless of disease severity, although it does not appear to be associated with a concomitant increase in mortality.[20]

Preventing exacerbations in COPD patients is a major treatment objective. Among the predominant triggers of exacerbations are LRTI, environmental contaminants, pollution, and poor compliance with pulmonary rehabilitation regimes or with long-term oxygen therapy.[21] However, approximately two-thirds of exacerbations are associated with bacterial or viral LRTI or bacterial colonization of the lungs,[1,5,22,23] and the spectrum of microorganisms associated with these infections appears to vary with disease severity.[24] In a study of hospitalized COPD patients, *Streptococcus* spp. were more prevalent in patients with less severe airway obstruction, whereas *Haemophilus* spp. were more prevalent in moderate disease and Enterobacteriaceae and *Pseudomonas* spp. in severe disease.[24] This finding suggests that pneumococcal vaccination should be envisaged particularly in patients with mild airflow obstruction.

Although there has been some debate on whether pneumonia should be considered a cause or differential diagnosis of acute exacerbation of COPD (AECOPD), another important observation is that pneumonic AECOPD tends to be more severe than nonpneumonic AECOPD. In analyses of COPD-related hospitalizations, pneumonic AECOPD in Denmark accounted for 36.1% of all first-time hospitalizations for AECOPD and resulted in more ICU admissions (12.5% vs 7.7%), longer median hospitalization stay (9 vs 5 days), and higher 30-day mortality (12% vs 8%) than nonpneumonic AECOPD (Figure 2A–C).[25,26] The severity of pneumonic AECOPD is further substantiated by a UK study that found in-hospital mortality and 90-day mortality to be significantly higher in patients with pneumonic AECOPD compared to patients with nonpneumonic AECOPD (Figure 2D)[27] and by a Serbian study that found pneumonia to be the second-most frequent autopsy-confirmed cause of death (28%) after heart failure (37%) in COPD patients who died within 24 hours of hospital admission.[28]

Pneumonia not only bodes poorly for the outcome of COPD patients but also has profound implications for health-care systems. Direct medical costs and productivity costs associated with hospitalization for CAP are twice as high in patients with COPD compared to those in patients with no comorbidity.[29] COPD patients with CAP are also ninefold more likely to be hospitalized and fourfold more likely to visit the ER, both of which drive the first-year health-care costs for these patients to an excess of US$22,348 over the costs of COPD patients without CAP.[6] Excess costs in COPD patients with CAP also remain high over the second year after hospitalization and have been estimated to be $6,000.[7]

In summary, the global burden of COPD is substantial, and the risk and frequency of pneumococcal pneumonia in these patients, as well as in others with multiple comorbidities, is many times higher than in healthy adults without comorbidities. Viral and bacterial pneumonic infections are a major cause of respiratory events in COPD patients. The outcomes of these infections tend to be more severe and more deadly than in COPD patients with nonpneumonic AECOPD, leading to longer, more expensive hospitalizations and greater overall costs. Preventing pneumonia in COPD patients could provide substantial benefits to these patients, as well as to the community.

Pneumococcal vaccines: clinical evidence of efficacy and recommendations

Multivalent pneumococcal polysaccharide vaccines (PPVs) have existed for many years, and the 23-valent vaccine (PPV23) is recommended by many public health agencies for adults ≥65 years of age and other high-risk groups. Its use comes with possible caveats, however, because the immunoresponses to PPV23 tend to wane over time, and demonstrations of clinical efficacy against CAP and IPD in at-risk populations have been inconsistent.[30–32]

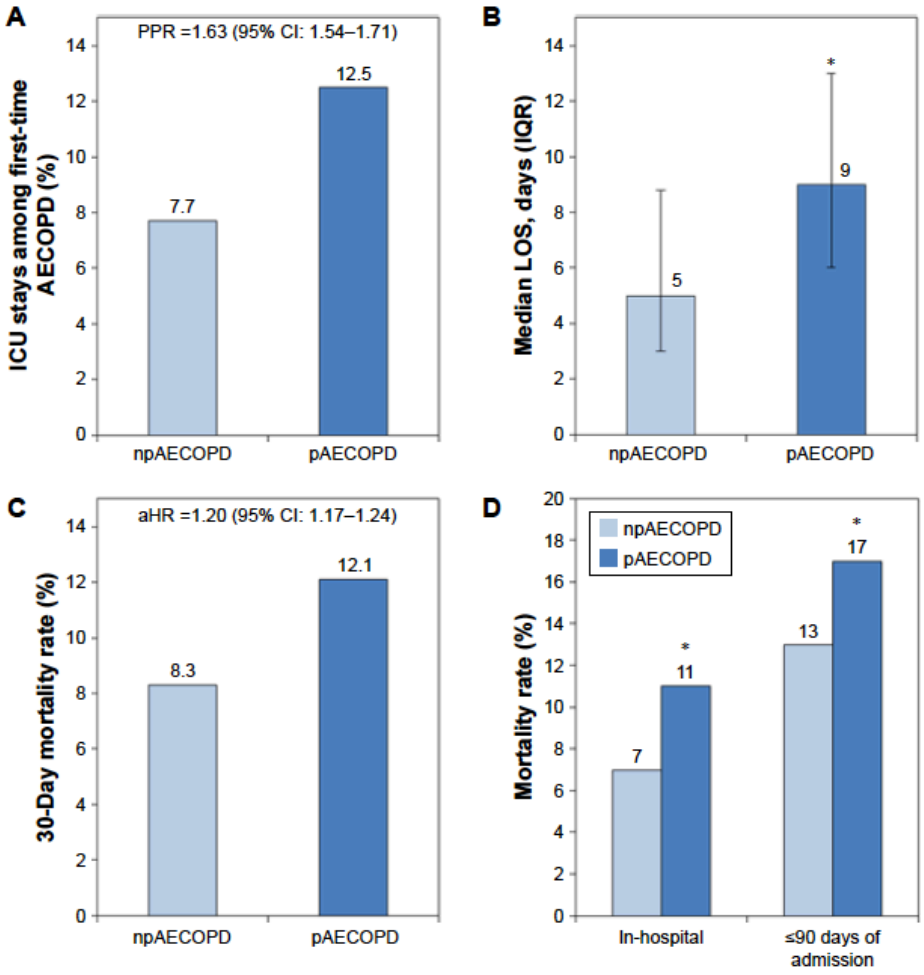


Figure 2 Intensive care unit (ICU) admissions, stays, and mortality of COPD patients with pneumonic and nonpneumonic exacerbations.
Notes: **(A)** Admission rates among 52,520 patients with a first-time hospitalization for acute COPD exacerbation (AECOPD), ≥40 years of age in Denmark, 2006–2012. The Danish National Patient Registry was used to identify all first-time inpatient hospitalizations for pneumonic AECOPD (pAECOPD; 18,968 patients) and nonpneumonic AECOPD (npAECOPD; 33,552 patients). All COPD hospitalizations were categorized according to whether they included a primary or secondary diagnosis of pneumonia. Data from Søgaard et al.[24] **(B)** Median ICU length of stay (LOS) in COPD patients due to pAECOPD or npAECOPD. Data were obtained from a retrospective analysis of all hospitalizations in 2005 in the departments of internal and respiratory medicine in one Swedish and two Norwegian hospitals. A total of 1,144 hospital admissions (731 patients) were identified from the patient administrative systems: 237 were for pAECOPD (mean age 75.3 years) and 472 for npAECOPD (mean age 71.7 years). *$P<0.001$. Data from Andreassen et al.[25] **(C)** 30-Day mortality among the 52,520 patients described in A, with adjustments for age, sex, comorbidity, and respiratory medications. Data from Søgaard et al.[24] **(D)** In-hospital and 90-day mortality in COPD patients following hospitalization for npAECOPD or pAECOPD in the UK in 2008. UK National COPD audit data were used to determine in-hospital and 90-day mortality rates of patients admitted with npAECOPD (542 of 7,833 patients and 951 of 7,504 patients, respectively) or pAECOPD (160 of 1,505 patients and 247 of 1,441 patients, respectively). A total of 9,338 admissions were assessed, with a mean age of 73 years. *$P<0.001$. Data from Myint et al.[27]

However, in a recently updated Cochrane meta-analysis published after our symposium, pneumococcal vaccination (primarily with PPV23) was associated with statistically significant efficacy against CAP and AECOPD in COPD patients.[33] In contrast, another recent review found the evidence for the clinical efficacy of PPV23 in high-risk and at-risk populations to be inconsistent, despite some short-term protection.[34] In view of the historically uncertain and variable clinical efficacy of PPV23, the World Health Organization and public health agencies in Europe and the US recognize that there remains an unmet medical need to protect older adults and high-risk groups against pneumococcal pneumonia.[35–38]

Overall, PCVs tend to be more consistently immunogenic than PPVs and to increase the duration and memory of antipneumococcal immunoresponses. Vaccination with

PPV produces an immunoresponse that is limited to B-cell stimulation and antibody production.[39,40] In contrast, PCVs contain pneumococcal polysaccharide antigens covalently linked to an immunogenic carrier protein that together induce T-cell-dependent humoral immunoresponses (Figure 3) and stimulate T cells to help B cells produce antibodies to the vaccine and generate immune memory.[40–43] These characteristics can improve the magnitude and duration of the initial immunoresponse and potentially allow the immune system to respond more effectively to subsequent exposure to vaccine-type (VT) pneumococcal strains. In studies that have compared humoral immunoresponses to PCV and PPV in normal vaccine-naïve adults or older adults, short-term immunoglobulin and functional antibody responses were generally superior with PCV.[40,44–46] This has also been demonstrated in COPD patients, in whom superior functional antibody responses persisted for at least 2 years.[47,48] In some studies, however, the in vitro B-cell-specific responses of older adults vaccinated with PCV or PPV23 did not differ significantly immediately after vaccination[49,50] or after 6 months.[45] In healthy adults, long-term immunoresponses with PPV23 remain above baseline for as long as 10 years, though booster immunizations are generally recommended after 5 years.[51] To our knowledge, the long-term immunogenicity of PCV in normal healthy adults beyond 2 years has not been reported, but significant immunoresponses are known to persist for up to 5 years in HIV-positive adults.[52]

PCVs are recommended for all children and have been shown to prevent nasopharyngeal carriage of VT strains and to protect children against mucosal diseases, IPD, and otitis media.[53–57] Childhood vaccination programs that include PCV have also demonstrated significant reductions in pneumococcal diseases in adults (herd protection) as an indirect consequence of lower pneumococcal carriage in children.[58,59]

CAPITA was conducted to assess the clinical efficacy of PCV13 in older adults. It was a large prospective randomized, placebo-controlled trial in >84,000 participants ≥65 years of age.[8] The primary outcome was the efficacy of preventing a first episode of VT CAP. With up to 5 years of follow-up, vaccine efficacy in the per-protocol population was 45.6% against VT CAP and 45% against abacteremic, noninvasive VT CAP (Figure 4). Vaccine efficacy was 30.6% against pneumococcal CAP and 75% against VT IPD. In an exploratory post hoc analysis of the at-risk population in the study, which included over 42% of the participants in each group, 10% of which had lung disease, vaccine efficacy was similar: 40.3% against VT CAP and 30.2% against pneumococcal CAP.[97] Furthermore, the magnitude and duration of humoral immunoresponses in at-risk adults assessed by opsonophagocytic assay geometric mean antibody titers were

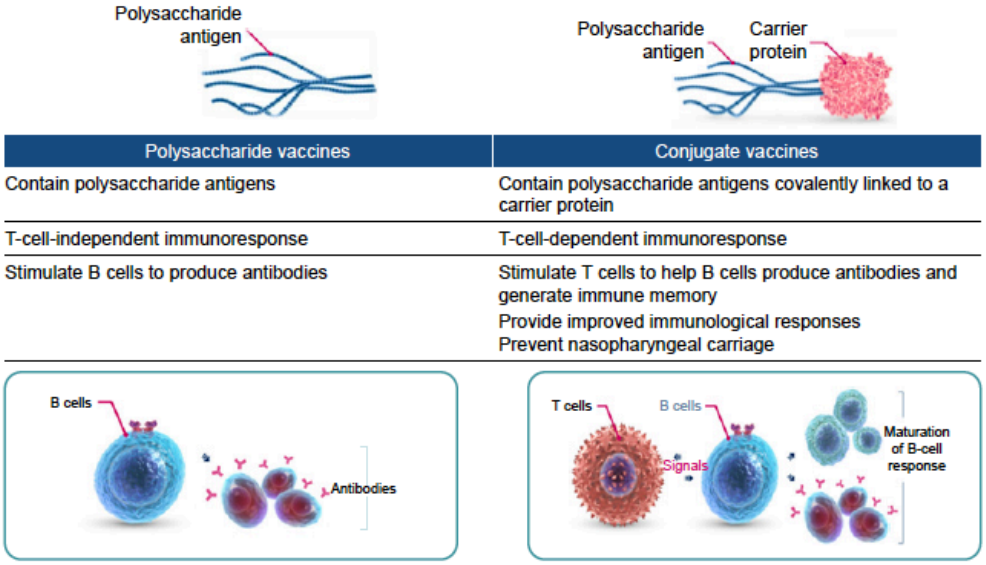


Figure 3 Immunogenic effects of pneumococcal vaccines.
Notes: Pneumococcal polysaccharide vaccines contain serotype-specific polysaccharide antigens only and induce T-cell-independent antibody production from B cells. These responses tend to wane over time. Pneumococcal conjugate vaccines contain serotype-specific polysaccharide antigens covalently linked to a carrier protein. These vaccines induce T-cell-dependent antibody production from B cells and improve immune memory, allowing antipneumococcal immunoresponses to be generated long after vaccination. Based on data from Clutterbuck et al,[41] de Roux et al,[40] Pollard et al,[45] and Siegrist.[42]

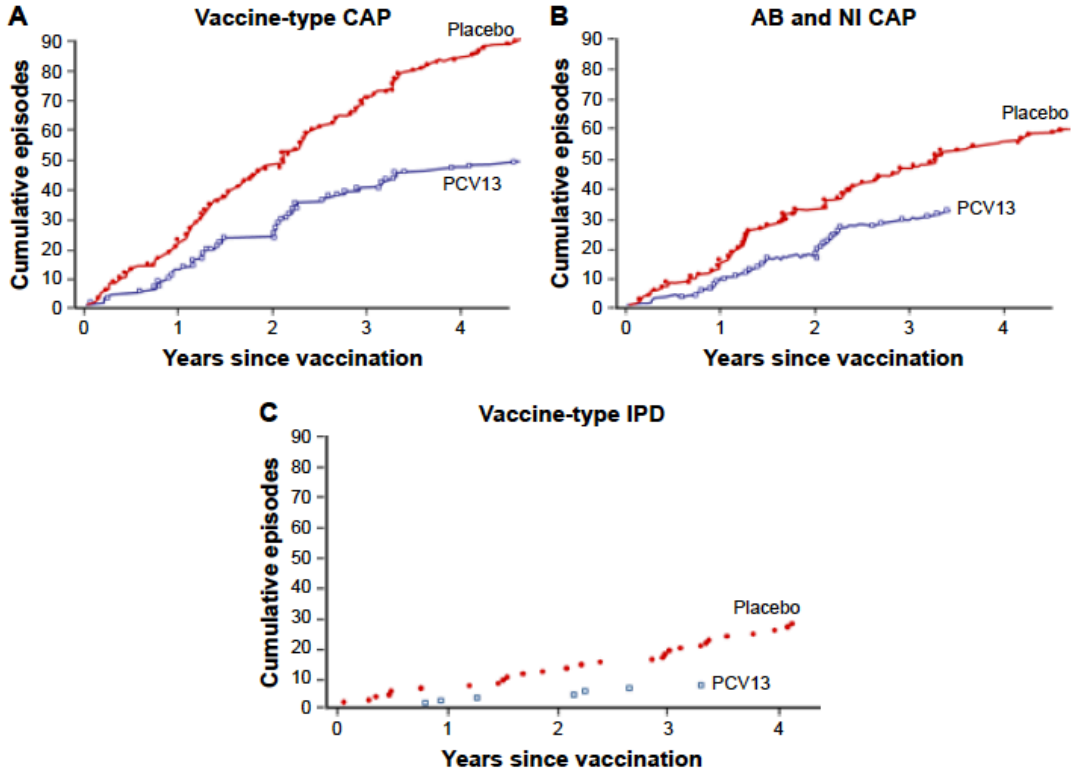


Figure 4 Efficacy of PCV13 in older adults: results of the CAPITA study.
Notes: CAPITA was a randomized, double-blind, placebo-controlled trial that evaluated the efficacy of 13-valent polysaccharide conjugate vaccine (PCV13) versus placebo in 84,496 adults ≥65 years of age. The primary objective was vaccine efficacy in preventing a first episode of vaccine-type pneumococcal community-acquired pneumonia (CAP). A secondary objective was vaccine efficacy in preventing a first episode of vaccine-type abacteremic (AB) and noninvasive (NI) pneumococcal CAP. The figure illustrates post hoc analyses of the cumulative episodes of primary and secondary efficacy end points in the per-protocol population. (**A**) Cumulative first episodes of vaccine-type CAP from vaccination to 5-year follow-up. Vaccine efficacy was 45.6% (95.2% CI: 21.8%–62.5%, $P<0.001$). (**B**) Cumulative first episodes of vaccine-type AB and NI CAP from vaccination to 5-year follow-up. Vaccine efficacy was 45% (95.2% CI: 14.2%–65.3%, $P=0.007$). (**C**) Cumulative first episodes of vaccine-type invasive pneumococcal disease (IPD) from vaccination to 5-year follow-up. Vaccine efficacy was 75% (95% CI: 41.4%–90.8%, $P<0.001$). From *N Engl J Med*. Bonten et al. Polysaccharide conjugate vaccine against pneumococcal pneumonia in adults. 372:1114–1125. Copyright © 2015 Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.[8]
Abbreviation: CAPITA, Community-Acquired Pneumonia Immunization Trial in Adults.

comparable to those of the overall population and persisted for at least 2 years.[60]

Finally, another post hoc analysis predicted that vaccine efficacy would decline from 65% for adults 65 years of age to 40% for adults 75 years of age, suggesting that patients with indications of PCV should be vaccinated as early as possible.[61] While these results are encouraging, post hoc analyses should be viewed with caution, and the efficacy of PCV13 for preventing VT CAP in CRD patients has yet to be demonstrated in a randomized clinical trial designed to address this issue specifically. It should be noted that in such a hypothetical trial, the necessary sample size to demonstrate efficacy is likely to be very large, and recruiting the minimum number of CRD patients for the treatment and control arms would be extremely difficult, especially in the context of populations benefiting from herd immunity arising from pediatric vaccination programs.

Recently published studies have also investigated the efficacy of PPV23 in older adults. A meta-analysis of 17 eligible studies in adults ≥60 years of age found pooled efficacies of PPV23 against IPD (45%–73%) and pneumococcal pneumonia (48%–64%) by any serotype.[62] Another meta-analysis of studies in adults ≥50 years of age also found evidence of significant vaccine efficacy for PPV23 against IPD (50%–54%) and against all-cause CAP (4%–17%).[63] Both studies concluded that efficacies of PPV23 and PCV13 against VT pneumococcal disease were comparable. In a multicenter prospective study in adults ≥65 years of age treated for CAP, PPV23 efficacy was 27.4% (95% CI: 3.2%–45.6%) against all pneumococcal pneumonia.[64]

The US Advisory Committee on Immunization Practices currently recommends PCV13 followed by PPV23 for all adults ≥65 years of age who have not previously received pneumococcal vaccine and in persons ≥19 years of age who

are at high risk of pneumococcal disease due to underlying medical conditions.[65,66] Several European scientific societies also recommend PCV13 for immunocompromised adults and all persons ≥65 years of age, along with at least one dose of PPV23 given 2–6 months afterward.[67] PCV13 is now being progressively implemented into national programs across Europe. As of August 2016, PCV13 is recommended for use in high-risk populations in >25 countries, for use in at-risk populations in >16 countries, and for use in older adults (>50 or >65 years of age) in >14 countries.

PCV13 is recommended to be given before PPV23.[66] This schedule is based on the observation that the responses to the serotypes common to both vaccines were stronger if PCV13 were administered first.[68] Of note, PCV13 can be given concomitantly with a seasonal inactivated influenza vaccine without impacting immunoresponses to either vaccine, which can help avoid missed opportunities for vaccination.[69,70]

In summary, PCV13 has been developed to provide improved protection for older adults and adults with chronic conditions, such as COPD, who are at high risk of pneumococcal infection and pneumonia. In the pivotal CAPITA study, PCV13 induced specific and efficacious immunoresponses in adults ≥65 years of age with or without underlying chronic conditions that elevate the risk of pneumonia, and vaccine efficacy against VT CAP and VT IPD persisted for up to 5 years. As a result, an increasing number of countries across Europe are including PCV13 in their vaccination recommendations.

Role of pneumococcal vaccination in patients with chronic respiratory diseases

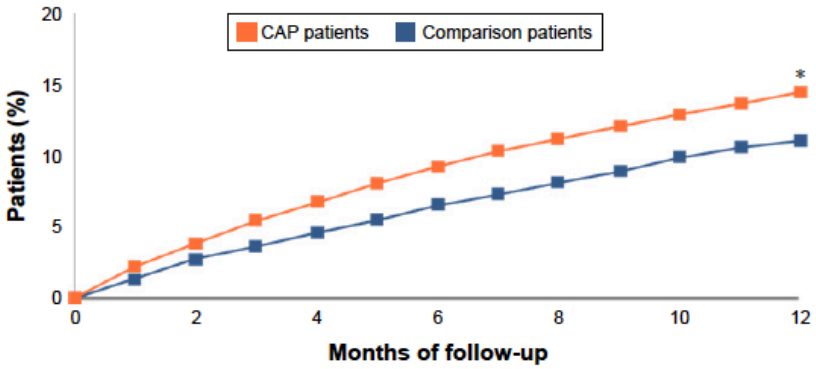
Current European Respiratory Society and European Society of Clinical Microbiology and Infectious Diseases guidelines were published before the recent results on PCV, and thus recommended only PPV23 for older adults and adults with risk factors for pneumococcal disease, such as age ≥65 years, congestive heart failure, COPD, and a previous history of pneumonia.[71] Specific recommendations on pneumococcal vaccination are lacking in many guidelines on CRDs from international societies. For COPD, pneumococcal vaccination is recommended in current GOLD guidelines, which mention the increased immunogenicity of PCV13, but do not propose a clear position on whether it should be preferred over PPV23.[72]

Because LRTIs are an important trigger for exacerbations, preventing them in COPD patients could also help prevent exacerbations.[5] Early prevention of exacerbations may also be critically important for preventing disease progression and subsequent events, as exacerbations can indicate or precede a feed-forward pattern of increased susceptibility to exacerbation and in some cases a frequent exacerbation phenotype.[21] In the natural history of COPD, each exacerbation is associated with an increased risk of subsequent exacerbations, which tend to occur with greater frequency and severity. It is well known that patients can enter a vicious cycle of infection, exacerbation, and disease progression.[3,4,73,74] With each exacerbation, further tissue destruction and functional impairment can occur along with worsening mucociliary clearance and increased bacterial colonization, all of which increase the risk of developing an LRTI and another exacerbation. The reality of this concept was further demonstrated by comparing the exacerbation frequencies of COPD patients after a CAP episode to those in COPD patients who had not had CAP (Figure 5). The cumulative risk of exacerbation in the first year after CAP was 1.5 times higher in patients who had had CAP (17%) compared to those who had not (11.4%; $P<0.001$).[96]

Clinical evidence of pneumococcal vaccine efficacy in COPD

In principle, pneumococcal vaccination should prevent LRTI and acute exacerbations in COPD patients, but interpreting the existing evidence for the clinical efficacy of PPV in these high-risk patients has been somewhat problematic. In a 2010 Cochrane systematic review and meta-analysis of seven studies,[32] the overall vaccine effect against pneumonia was of borderline significance compared to placebo, with an OR of 0.72 (95% CI: 0.51–1.01), with no significant effects on either exacerbations or cardiorespiratory mortality. While these results suggested that PPV may confer some protection in COPD patients, the lack of statistical significance for any outcome and the heterogeneity of the studies rendered the evidence inconclusive. The evidence for vaccine efficacy improved somewhat in the 2017 update of this Cochrane review, which included a reanalysis of the same studies used in the 2010 meta-analysis of pneumococcal vaccination efficacy (primarily PPV23) against CAP, and concluded that vaccination was associated with significant reductions in the likelihood of experiencing CAP (OR: 0.62, 95% CI: 0.43–0.89) or AECOPD (OR: 0.6, 95% CI: 0.39–0.9).[33]

A recent review of pneumococcal vaccine efficacy studies in persons with underlying risk factors, such as COPD or a CRD, vaccine efficacy against any-cause CAP was found to vary widely between –338% and 43%, with an overall efficacy of 29% (95% CI: –39%–63%) in adults aged ≥50 years with CRD.[34] In a randomized controlled trial in 596 COPD patients, PPV23 efficacy against CAP was significant at 76% (95% CI: 20–93, $P=0.013$) in patients <65 years of age, nearly significant at 48% (95% CI: 27–80, $P=0.076$) in those with severe airflow obstruction (<40% FEV_1), and



Number of patients at risk							
CAP patients	8,274	7,493	6,891	6,384	5,908	5,412	4,984
Comparison patients	8,274	7,715	7,273	6,847	6,372	5,889	5,460
Percentage with a subsequent exacerbation							
CAP patients	–	3.9%	6.8%	9.3%	11.2%	12.9%	14.6%
Comparison patients	–	2.8%	4.7%	6.6%	8.1%	9.9%	11.2%

Figure 5 Community-acquired pneumonia (CAP) and occurrence of subsequent exacerbations in COPD patients in the US, 2010.
Notes: In a retrospective cohort study of 12,327 matched pairs, CAP patients aged ≥18 years who had continuous and comprehensive health benefits, evidence of COPD, and no evidence of pneumonia during the preceding year were identified between January and December 2010. One comparison patient from the corresponding source population who had continuous and comprehensive health benefits, evidence of COPD, and no evidence of pneumonia during the preceding year was matched with each CAP patient on the date of the initial CAP encounter (or inpatient admission date) or within the next 30 days. Comparison patients were also matched with each CAP patient on age (±1 year), sex, and selected markers of health status measured in the preceding year. Exacerbation was defined as a hospitalization or emergency department visit during follow-up, which began 30 days after pneumonia diagnosis and ended 12 months later. *P<0.001. From Weycker et al;[*] reprinted with permission from the authors.

strongest for both factors combined (91% [95% CI: 35–99, *P*=0.002]).[75] However, vaccine efficacy was not significant for the overall cohort (24% [95% CI: –24–54, *P*=0.333]).

In a study of the combined efficacy of PPV23 and influenza vaccination in preventing acute exacerbation in adult CRD patients, acute exacerbation frequency was significantly lower in the PPV23 + influenza vaccination group than in the influenza vaccination-alone group (*P*=0.022), and there was a significant additive effect of PPV23 in COPD patients (*P*=0.037).[76] In view of the limited numbers of studies available to date, the evidence on the role of PPV for protecting COPD patients from CAP can be considered inconsistent.

In contrast, seasonal influenza vaccine has demonstrated significant efficacy in preventing exacerbations in COPD patients compared to placebo, with a reported weighted mean difference between treatments of –0.37 (95% CI: –0.64 to –0.11, *P*=0.006) in a meta-analysis of two randomized trials.[77] If influenza vaccine is administered concomitantly with PPV23, the two vaccines provide an additive effect in reducing the risk of hospitalization for pneumonia, death, death from influenza, and death from pneumonia.[78–80]

Another potential benefit of an effective pneumococcal vaccination could be a reduction in antibiotic treatments. This has not been studied in COPD patients, but has been estimated in children by comparing antibiotic treatment days for *S. pneumoniae* infections in countries with high childhood PCV coverage versus countries without such coverage.[81] Globally, an estimated 11.4 million antibiotic treatment days were avoided in countries with PCV coverage, a reduction of 47%. Reducing antibiotic treatment in COPD patients could also help delay or prevent colonization of the lungs by antibiotic resistant bacteria.

Real-life vaccine coverage of the target population

Despite the availability of effective pneumococcal vaccines and recommendations from most national health authorities, coverage remains suboptimal in many settings. Recent coverage rates have been fairly high in the UK (70% in persons ≥65 years of age in 2014–2015) and in Spain (76% in persons ≥60 years of age in 2010), lower in Ireland (36% in persons ≥65 years of age and 18% in high-risk adults in 2013), and very low in Norway (15%–30% in persons ≥65 years of age in 2014–2015), Germany (15% in high-risk persons in 2014), and France (~5% in persons ≥65 years of age in 2010–2011).[82–87]

An indication of the reasons behind these suboptimal coverage rates may lie in the perceptions and vaccine awareness of older adults. A recent survey (PneuVUE, Pfizer, Paris, France) measured public awareness of pneumonia and vaccine perceptions in adults ≥50 years of age across nine EU countries.[88] The survey found that 85% of these adults trusted vaccines, 27% avoided vaccines (for safety reasons), and 29% feel they "didn't need" vaccines because they were not at risk. However, high proportions of respondents reported that they did follow their physician's advice (92%) and that they preferred to obtain additional medical information from their doctor (92%). Overall, pneumococcal vaccine awareness was low, and the most frequent reason given (55%) for not being vaccinated was that it was never offered by their doctor.

To summarize, evidence-based guidelines recommend pneumococcal vaccination in persons with CRD, and PCV13 has already been included in a number of national recommendations, including those in the US, France, Portugal, Spain, Italy, and others.[66,89–92] Some countries, such as Germany and the UK, continue to consider the evidence and favor the broader serotype coverage of PPV23.[93,94] In patients with COPD, preventing LRTIs, which frequently involve *S. pneumoniae*, appears critical, because they can alter disease status and speed disease progression, thus increasing the risk of subsequent exacerbation. Including pneumococcal vaccination in early care for COPD may improve the long-term natural history of the disease, although further evidence is needed. Despite recommendations, overall pneumococcal vaccination coverage is poor across Europe and public awareness and knowledge of pneumococcal disease and vaccines is low. Since patients rely on their physicians as the main source of health information, physicians need to do a better job of informing their at-risk patients about the dangers of pneumonia and the benefits of pneumococcal vaccination.

Conclusion

Global CRD burdens are high and contribute to substantial excess health-care use, hospitalizations, and global morbidity and mortality.[72] Patients with COPD and other CRDs are at high risk of CAP, IPD, and exacerbations that further increase health-care burdens and mortality.[12,13] In COPD, airway infections are important triggers of exacerbations and hasten disease progression. There is evidence for the efficacy of PPV23 in older adults,[62,63] but evidence for protection in CRD patients has been considered inconclusive.[32] The CAPITA study provided clinical evidence that PCV13 is effective at preventing CAP in older adults, including those with comorbidities.[8] Post hoc analyses of CAPITA are consistent with PCV13 efficacy in patients with comorbidities, but these results should be viewed with caution. Indeed, vaccine efficacy in adults is likely to vary according to the pneumococcal vaccines used in pediatric vaccination programs and efficacy may be low or difficult to demonstrate in settings where pediatric uptake of pneumococcal vaccine is high and the consequent burden of disease in adults is reduced.[95] However, given the substantially higher risk of respiratory infection and dire consequences of such infections in patients with COPD or CRD, vaccination is warranted in these patients, regardless of the level of herd protection present in the community.

Influenza and pneumococcal infections are important contributors to CAP and acute exacerbations in COPD patients, and pneumococcal and influenza vaccinations together may have an additive preventive effect.[78–80] Vaccination early in the course of COPD could help maintain stable health status, although further demonstration is needed.[5,21] Despite the great burden of pneumonia and pneumococcal infection, the need for vaccination in patients with CRD–COPD, the evidence on pneumococcal vaccine efficacy, and widespread national recommendations, improvements are needed in pneumococcal vaccine coverage, knowledge, and awareness.[88] As the main source of medical information for the public, physicians need to communicate more effectively the benefits of vaccination with PCV to their patients, especially those with CRDs.

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6. Discussão dos resultados

Como já foi referido, no âmbito da tese sobre o impacto dos internamentos de adultos por PAC em Portugal continental, identificaram-se os seguintes objetivos principais e secundários:

1. Objetivos principais:
    1.1. Incidência dos internamentos de adultos por PAC em Portugal continental
    1.2. Letalidade intra-hospitalar dos internamentos de adultos por PAC em Portugal continental
    1.2. Letalidade intra-hospitalar dos internamentos de adultos por PAC em Portugal continental
    1.3. Custos diretos dos internamentos de adultos por PAC em Portugal continental
2. Objetivos secundários
    2.1. Papel dos médicos na decisão crítica de internamento hospitalar por PAC
    2.2. Importância das medidas de promoção da saúde e de prevenção da doença na redução do impacto dos internamentos de adultos por PAC em Portugal continental

6.1. Discussão dos objetivos principais

Incidência dos internamentos de adultos por PAC em Portugal continental

No período de 2000 a 2009, foram avaliados 294.027 internamentos de adultos com o diagnóstico principal de PAC. Os internamentos ocorreram predominantemente em indivíduos do género masculino (56%) e idosos. A média da idade dos doentes internados foi de 73,1 anos, com 71,3 anos para os homens e 75,3 anos para as mulheres. Durante a década analisada, verificou-se um aumento consistente na média anual da idade dos doentes internados, mais evidente nos grupos etários mais idosos. Verificaram-se internamentos em todas as idades dos 18 aos 109 anos e, apesar do peso da idade, 10,3% dos internamentos ocorreram em adultos com idade <50 anos.

Estes internamentos correspondem a 3,7% do total de internamentos de adultos no SNS, aumentando para 5,5% e 7,0% na população com idade ≥50 anos e ≥65 anos, respetivamente.

Foi, igualmente, constatado no período analisado um aumento do número de internamentos em todos os grupos etários, independentemente do género, mais marcado nas idades ≥65 anos.

Estes internamentos correspondem a uma incidência média anual de 3,61 internamentos por 1.000 habitantes, com uma distribuição desigual por grupos etários, bem patente no valor de 0,66 na população com idade <50 anos, 7,49 na população com idade ≥50 anos e 13,40 por 1.000 na população com idade ≥65 anos. O aumento do número de internamentos teve necessariamente impacto na incidência com um acréscimo de 28,3%, de 3,16 por 1.000 no período de 2000 a 2004 para 4,05 por 1.000 habitantes de 2005 a 2009.

Estes dados corroboram o impacto dos internamentos por PAC no SNS, com valores dentro dos intervalos de referência das incidências encontrados em estudos similares no Reino Unido (1), Alemanha (2) e Dinamarca (3). Confirma-se, igualmente, o predomínio de internamentos nos homens (2) e o aumento muito significativo da incidência dos internamentos hospitalares com a idade (1-4). Contudo e a merecer uma melhor análise em estudos subsequentes, de referir que na população com idade ≥65 anos, a incidência dos internamentos em Portugal foi de 13,4 por 1.000, um valor que compara menos favoravelmente com um estudo de menor dimensão e duração (2002-2005) realizado na província de maior rendimento em Espanha, a Catalunha de 10,5 por 1.000 (4).

À semelhança dos valores documentados em outros estudos europeus de grande dimensão (1-3), em Portugal verificou-se, igualmente, um aumento significativo da incidência dos internamentos por PAC ao longo do período de 10 anos analisado. Todos estes estudos europeus (1-3), divergem da tendência em sentido contrário verificada nos EUA de diminuição da incidência de 26,7 por 10.000 adultos em 1991 (5) para 24,8 por 10.000 em 2010-2012 (6). Contudo neste estudo (6), o período analisado é de menor duração e limitado de janeiro de 2010 a junho de 2012.

Comparativamente com o outro estudo realizado em Portugal continental no período de 1998 a 2000 (7), verifica-se que, em relação ao período agora analisado de 2000 a 2009, ocorreu um aumento da percentagem total de internamentos de 3,0%, para 3,7% e da incidência de 2,66 internamentos por 1.000 para 3,61 por 1.000 habitantes.

Os dados apurados neste estudo que analisa o período de 2000 a 2009 permitem fundamentar que em média, em Portugal continental, verificam-se 81 internamentos de adultos por PAC por dia, o que corresponde a um internamento a cada 18 minutos.

Letalidade intra-hospitalar dos internamentos de adultos por PAC em Portugal continental

Relativamente à mortalidade, verificaram-se 59.925 óbitos, o que corresponde a uma taxa de letalidade intra-hospitalar de 20,4%. Verificaram-se óbitos em todos os grupos etários, com a particularidade do valor de letalidade intra-hospitalar mais baixo ter sido de 1,7% nos doentes internados com idade igual a 29 anos. Como está documentado em todos os estudos, a letalidade aumentou significativamente com a idade com valores médios de 5,0% nos doentes com idade <50 anos, 7,5% nas idades <65 anos, 11,4% nas idades <75 anos e 24,1% e 26.8% nos doentes com idade ≥65 anos e ≥75 anos, respetivamente. A letalidade aumentou ao longo dos dez anos estudados após ajustamento para a idade e sexo. A média das idades dos doentes falecidos foi de 79,8 anos, significativamente mais elevada do que a dos doentes não falecidos (71,3 anos). Os doentes com idade ≥50 anos apresentaram um risco relativo de morte intra-hospitalar de 4,4 comparando com os doentes com idade <50 anos. Nos doentes com idade ≥65 anos o risco relativo de morte intra-hospitalar foi de 3,2 vezes em comparação com os doentes com idade <65 anos. Os homens morreram mais e mais jovens do que as mulheres. O risco relativo dos homens falecerem foi 17% mais elevado em relação às mulheres, após ajustamento para a idade e o ano de internamento e a idade média dos homens falecidos foi de 78,1 anos, significativamente inferior à média da idade das mulheres falecidas de 82,1 anos.

Estes valores de letalidade intra-hospitalar estão englobados nos valores de referência da revisão abrangendo nove países europeus e publicada em 2012 (8). Contudo, de acordo com estudos apresentados pela BTS nas suas recomendações de 2009 (9), a letalidade intra-hospitalar no Reino Unido apresenta valores mais baixos entre os 8 e os 14%.

No nosso estudo, confirma-se igualmente o aumento das taxas de letalidade associadas ao envelhecimento da população (10). Embora os dados não possam ser diretamente comparáveis, de referir que, ao contrário do verificado nos países europeus, nos EUA a mortalidade por PAC desceu para valores históricos inferiores a 20 óbitos por 100.000 habitantes (11). Esta diminuição foi atribuída à vacinação por rotina das crianças com a VPC13 e à maior transparência e divulgação pública do processo de cuidados e das taxas de readmissão e mortalidade (11).

Comparativamente com o outro estudo realizado em Portugal continental no período de 1998 a 2000 (7), verifica-se, em relação ao período agora analisado de 2000 a 2009,

um acréscimo da letalidade intra-hospitalar de 17,3% para 20,4% e no grupo etário com idade ≥65 anos de 21,5% para 24,1%.

Os dados apurados neste estudo que analisa o período de 2000 a 2009 permitem fundamentar que em média, em Portugal continental, verificam-se 16 óbitos por dia, no decurso dos internamentos de adultos por PAC, o que corresponde a um óbito a aproximadamente cada 90 minutos.

Custos diretos dos internamentos de adultos por PAC em Portugal continental

Os custos diretos dos internamentos de adultos por PAC foram calculados pela tabela de preços a praticar pelo SNS, de acordo com a portaria que define os valores para os Grupos de Diagnóstico Homogéneo e de acordo com o respetivo ano de internamento. No cálculo dos custos diretos estão incluídos todos os doentes internados, independentemente do local de internamento, ou seja, os doentes com internamentos em enfermaria e em UCI.

No período de 2000 a 2009, os custos diretos globais foram aproximadamente de 800 milhões de euros, o que corresponde a uma média anual de 80 milhões de euros e a uma média diária de 218.050 euros, com tendência crescente ao longo dos anos. Cada internamento teve um custo direto médio de 2.706 euros. Na análise por resultados, a média do custo diário por internamento com alta vivo foi de 2.515 euros e falecido foi de 3.457 euros, um acréscimo de 37,5%. Na pesquisa da literatura efetuada não encontramos dados relativos a custos diretos de acordo com o resultado de internamento, o que nos impede de comparar com os valores do estudo. Admitimos que o custo dos doentes falecidos seja mais elevado em virtude do maior consumo de recurso e, muito provavelmente, necessidade de internamento em UCI.

A inclusão dos doentes com internamento em UCI pode, igualmente, ter contribuído para um custo direto médio superior aos valores referidos de €1.553 na Espanha (12), de €1.201 Alemanha (13) e de €1.586 na Itália (14).

Os dados apurados neste estudo que analisa o período de 2000 a 2009 permitem fundamentar que em média, em Portugal continental, os custos diretos dos internamentos por PAC somam um milhão de euros a cada 4 dias e 14 horas

Limitações da metodologia utilizada

Os quatros artigos apresentam várias limitações. Em primeiro lugar, os artigos n.º 1, 3 e 4 por serem retrospetivos e utilizarem a base de dados administrativa com informação codificada da nota de alta dos internamentos hospitalares. Contudo em Portugal, a codificação é feita exclusivamente por médicos com formação específica, sendo realizadas auditorias periódicas, internas e externas, ao processo de codificação o que pode contribuir para um maior rigor. Devido à inexistência na ICD-9-CM de um código específico para PAC, neste estudo foram apenas analisados os internamentos de adultos com o diagnóstico principal de pneumonia. Não se incluíram doentes com os diagnósticos principais de falência respiratória ou choque séptico associados a um diagnóstico secundário de pneumonia, que podem estar relacionados com taxas de letalidade intra-hospitalar mais elevadas (15), mas também a casos de pneumonia nosocomial. Admite-se, contudo, a inclusão na população analisada de alguns casos de pneumonia adquirida em meio hospitalar por erro de codificação ou porque a base de dados não permite identificar os reinternamentos por pneumonia após alta hospitalar recente. A base de dados também não permite identificar os doentes residentes em lares ou instituições de cuidados continuados de longa duração, pelo que é expectável que tenham sido incluídos casos de pneumonia associada a cuidados de saúde, sobretudo nos mais idosos. No entanto, este conceito e a sua inclusão na pneumonia nosocomial não é consensual e para alguns autores não está validado na Europa (16). A maior acessibilidade às instituições hospitalares e o receio de falecer inadequadamente no domicílio, quer dos doentes quer dos seus familiares, podem justificar a inclusão no estudo de doentes com pneumonia de fim de vida. Estes casos podem ter maior representatividade e impacto nos grupos etários mais idosos.

De referir que a metodologia utilizada permitiu excluir os doentes com pneumonia tuberculosa ou obstrutiva, infetados com o vírus da imunodeficiência humana, transplantados e internados com causa externa de doença por antineoplásicos ou imunossupressores. Contudo, a metodologia não permite identificar o subgrupo de doentes que necessitaram de admissão em UCI. De igual modo, na nossa base de dados não estava disponível informação sobre a gravidade dos episódios de pneumonia, hábitos tabágicos e etanólicos ou estado vacinal, nomeadamente contra a gripe e doença pneumocócica. Apesar destas limitações, a metodologia utilizada tem sido considerada válida e aplicada em múltiplos estudos realizados em diferentes países (1,17-19).

Estes três artigos apresentam a vantagem de analisar um período de 10 anos, facto que permite minimizar o impacto dos anos que se desviam da normalidade, como o de 2009,

em que ocorreu a pandemia de gripe A(H1N1). No ano de 2009 e comparativamente com os anos anteriores ocorreram mais internamentos por pneumonia, o que poderá ter ocorrido em consequência da pandemia de gripe. A pandemia de gripe não parece ter tido um impacto significativo na letalidade intra-hospitalar que foi inferior em 2009 em relação aos anos anteriores, embora possa ter contribuído para a diminuição da média das idades dos doentes internados e falecidos verificada nesse ano. De referir que em Portugal os dados oficiais apontam para uma mortalidade atribuível à pandemia de 124 óbitos (1,17 óbitos por 100.000 habitantes) com uma média de idades de 47,6 anos (20).

O período analisado termina em 2009, pelo que se admite que estes dados poderão já não estar totalmente atualizados. Fica o desafio da sua análise comparativa com o período de 2010 a 2019.

Relativamente ao artigo de revisão (artigo N.º 2), apesar de se ter incluído a PubMed da *US National Library of Medicine National Institutes of Health*, as fontes de informação não foram extensivas pelo que admitimos que alguns artigos com dados eventualmente relevantes podem não ter sido acedidos. Contudo, os artigos mais importantes e necessariamente indexados na PubMed foram analisados e incluídos.

6.2. Discussão dos objetivos secundários

Papel dos médicos na decisão crítica de internamento hospitalar por PAC

A decisão de internar um doente com PAC tem múltiplas e profundas implicações em termos de metodologia diagnóstica, abordagem terapêutica, alocação de recursos e prognóstico. Internar indevidamente um doente sem critérios de gravidade corresponde a um acréscimo muito significativo de custos, com exposição do doente a eventuais complicações hospitalares, como por exemplo, infeções nosocomiais e tromboembolismo venoso associado ao acamamento.

De igual modo, não internar um doente com critérios de gravidade ou sem condições de tratamento adequado ou em segurança no ambulatório, por exemplo, por falta de apoio familiar ou social, significa uma má decisão clínica com risco de vida para o doente e, previsivelmente, com maiores custos em resultado da deterioração do quadro clínico do doente e da necessidade de um internamento mais tardio, com maior gravidade e em piores condições.

A decisão de internar é, assim, um momento crítico na gestão do processo do doente e obriga a uma correta estratificação da gravidade do doente e, caso a situação o justifique, à identificação das condições que assegurem o cumprimento da terapêutica, com a vigilância e segurança adequadas. A complexidade da decisão tem fomentado o

desenvolvimento de índices e scores, dos quais os dois mais conhecidos são o PSI (21) e o CURB-65 (22). Apesar da utilidade, estes dois scores têm várias limitações. Nenhum dos scores tem em consideração fatores sociais, o estado funcional e, na avaliação das comorbilidades, a presença de DPOC ou imunossupressão. Quer a DPOC, quer a imunossupressão estão associadas a um risco acrescido de gravidade, por exemplo, a ocorrência de bacteriemia (23), e a sua presença não deve ser ignorada ou desvalorizada. De igual modo, nenhum dos scores está validado em populações de doentes residentes em Portugal. Estas circunstâncias não inviabilizam a utilização dos scores, mas não podem substituir o raciocínio e o senso clínico aplicado à resolução de cada caso individualmente.

Justifica-se, deste modo, que a decisão de internamento seja feita por médicos com maior experiência e diferenciação (SMART-DOCTORS).

Importância das medidas de promoção da saúde e de prevenção da doença na redução do impacto dos internamentos de adultos por PAC em Portugal continental

A dimensão dos internamentos de adultos com PAC, a par do seu contributo para o crescente problema das resistências aos antimicrobianos, justificam amplamente a adoção de medidas de promoção da saúde e de prevenção da doença. Os dados apresentados nos objetivos principais vêm documentar de uma forma muito significativa a morbilidade, a mortalidade e o consumo de recursos verificados em Portugal continental. O envelhecimento da população e a prevalência crescente de comorbilidades tornam ainda mais premente a intervenção junto de fatores de risco associados a estilos de vida e a vacinação contra a gripe e as infeções pelo *Streptococcus pneumoniae*.

Com a criação do acrónimo ATCHIN, um acrónimo simples e de fácil memorização, tentámos aglutinar um conjunto de intervenções no consumo moderado de bebidas alcoólicas, na cessação tabágica, na promoção do controlo das comorbilidades e da higiene oral, no uso criterioso de terapêuticas imunossupressoras e no reforço do adequado estado nutricional. A importância destes fatores de risco nas infeções respiratórias e, em particular, nas pneumonias está amplamente documentada em vários artigos de revisão (24,25).

Tanto quanto é do nosso conhecimento, não existia um acrónimo com estas características e objetivo e, embora a sua utilidade seja maior nos países de língua portuguesa, pensamos que poderá ser útil noutros países e noutras regiões fora do espaço da lusofonia. Esperamos que a simplicidade e a sonoridade sejam fatores de

sucesso na sua implementação e, consequente, intervenção nos principais fatores de risco associados a estilos de vida com impacto nas infeções respiratórias.

A importância da vacinação contra a gripe e infeções a Pneumococcus está totalmente justificada nos documentos orientadores e normativos da DGS. Contudo, o envolvimento das sociedades científicas é essencial para uma maior divulgação e implementação das orientações e normas nacionais. Com a elaboração do documento de consenso para a prevenção das infeções respiratórias no adulto, a Sociedade Portuguesa de Pneumologia pretendeu contribuir, de uma forma muito significativa, para uma maior consciencialização do problema das infeções respiratórias e da importância da sua prevenção. De referir que a Sociedade Portuguesa de Pneumologia congrega não só todos os médicos pneumologistas nacionais, mas também médicos de outras especialidades, tais como, de medicina geral e familiar, bem como outros profissionais de saúde, como, por exemplo, enfermeiros, fisioterapeutas e outros técnicos superiores de diagnóstico e terapêutica.

Dentro das patologias com risco acrescido para o desenvolvimento e gravidade da PAC e, necessariamente, associada a maior morbilidade, mortalidade e consumo de recursos, destaca-se a DPOC (23). Infelizmente a sensibilização destes doentes para a maior frequência e gravidade da pneumonia, associada a maior progressão da doença pulmonar, é inferior ao desejável, traduzindo níveis de cobertura vacinal subótimos. Os doentes com DPOC representam um subgrupo de doentes em que a intervenção nos fatores de risco e o aumento das coberturas vacinais têm maior influência na gestão e progressão da doença, no prognóstico e na alocação de recursos. Os profissionais de saúde devem estar atentos a esta realidade e aproveitar todas as oportunidades para um maior envolvimento dos doentes na gestão da sua doença. Foi com este objetivo que, em conjunto com reconhecidos líderes de opinião internacionais, publicámos um artigo de revisão sobre a vacinação pneumocócica em doentes respiratórios crónicos.

Limitações da metodologia utilizada

Os 4 artigos de revisão, opinião e de consenso necessitaram de uma revisão da literatura publicada sobre o assunto. Nesta revisão e apesar de ser ter incluído a PubMed da *US National Library of Medicine National Institutes of Health*, as fontes de informação não foram extensivas pelo que admitimos que alguns artigos com dados eventualmente relevantes podem não ter sido consultados. Contudo, os artigos mais importantes e necessariamente indexados na PubMed foram analisados e incluídos.

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7. Conclusões e perspetivas futuras

O impacto dos internamentos de adultos por PAC em Portugal continental é muito significativo em termos de morbilidade, mortalidade e consumo de recursos de saúde. No período de dez anos analisados, entre 2000 e 2009, verificaram-se 294.027 internamentos de adultos com o diagnóstico principal de PAC. Estes internamentos corresponderam a 3,7% do total de internamentos de adultos no SNS, em 56% ocorreram em homens e a média de idades dos doentes internados foi de 73,1 anos. Estes internamentos representam uma incidência média anual de 3,61 internamentos por 1.000 habitantes, com um aumento constante durante o período analisado.

Ocorreram 59.925 óbitos, o que corresponde a uma taxa de letalidade intra-hospitalar de 20,4%, com óbitos em todos os grupos etários. A média das idades dos doentes falecidos foi de 79,8 anos. Os doentes com idade ≥50 anos apresentaram um risco relativo de morte intra-hospitalar de 4,4 comparando com os doentes com idade <50 anos. Os homens morreram mais e mais jovens do que as mulheres com um risco relativo de falecerem 17% mais elevado do que em relação às mulheres. A letalidade aumentou ao longo dos dez anos estudados após ajustamento para a idade e sexo.

Os custos diretos globais foram aproximadamente de 800 milhões de euros, o que corresponde a uma média anual de 80 milhões de euros e a uma média diária de 218.050 euros, com tendência crescente ao longo dos anos. Cada internamento teve um custo direto médio de 2.706 euros. A média do custo diário por internamento com alta vivo foi de 2.515 euros e falecido foi de 3.457 euros, um aumento de 37,5%.

Os dados apurados neste estudo, permitem fundamentar que em média, em Portugal continental, verificam-se 81 internamentos de adultos por PAC por dia, o que corresponde a um internamento a cada 18 minutos. Nestes 81 internamentos diários, ocorreu o óbito em 16 doentes, um óbito a aproximadamente cada 90 minutos. E os custos diretos dos internamentos representaram um milhão de euros a cada 4 dias e 14 horas.

Tendo em consideração o impacto no prognóstico e nos custos, a decisão de internar adultos com PAC deve ser feita por médicos com maior experiência e diferenciação, que no seu raciocínio clínico devem ter em ponderação, além da estratificação da gravidade, a especificidade individual e a valorização do estado funcional e de fatores sociais.

A dimensão dos internamentos de adultos por PAC no nosso país, justifica decisivamente a intervenção nos principais fatores de risco associados a estilos de vida

e uma maior sensibilização da população e dos profissionais de saúde para o aumento das taxas de cobertura vacinal contra a gripe e as infeções por *Streptococcus pneumoniae*. O acrónimo ATCHIN pretende facilitar a intervenção nos principais fatores de risco associados a estilos de vida. O envolvimento das sociedades científicas é crucial na maior divulgação e implementação das recomendações nacionais de vacinação antigripal e antipneumocócica, elaboradas pelas DGS, e os doentes com DPOC representam um subgrupo de doentes em que a prevenção das pneumonias tem maior influência na gestão e progressão da doença, no prognóstico e na alocação de recursos. Na figura 3 apresentam-se as conclusões integradas no esquema conceptual da tese.

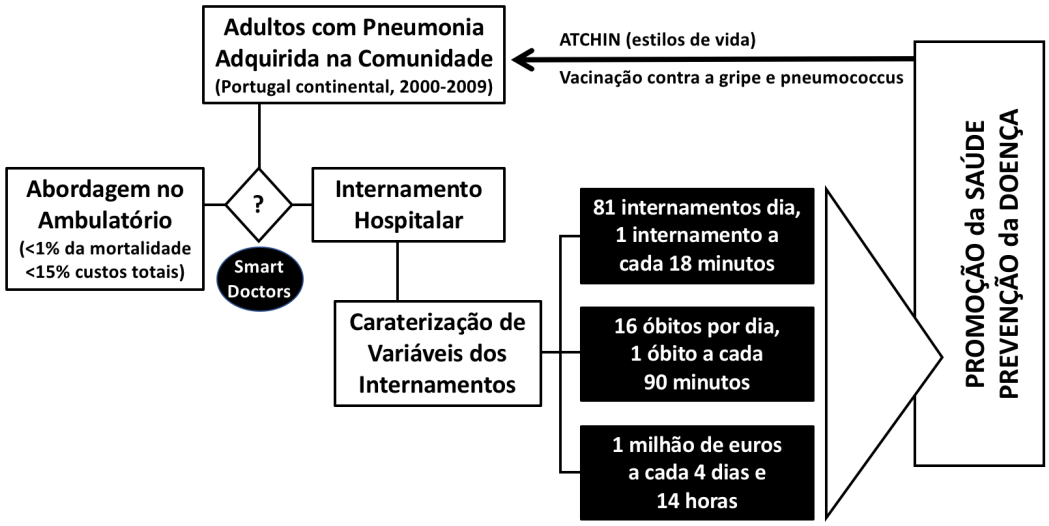

Figura 3 – Esquema conceptual da tese com as respetivas conclusões.

O envelhecimento da população, a par do aumento da prevalência das doenças crónicas não transmissíveis, está associado a um aumento dos internamentos por PAC. Esta tendência foi documentada ao longo do período agora analisado de 2000 a 2009. Justifica-se, deste modo, a monitorização periódica das variáveis analisadas nesta tese de modo a permitir uma melhor gestão desta entidade nosológica e dos seus internamentos, avaliar o impacto das intervenções preventivas e identificar outras medidas que se revelem úteis.

E é o nosso objetivo assim proceder.